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Comparative Inhalation Toxicology of Selected Materials

Final Report for Phase III Studies

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A subchronic inhalation study of powdered Cu-Zn alloy (Cu-Zn) was conducted with F344/N rats. Exposures were 1.5 hours/day, 4 days/week to 0, 0.32, 1.0, 3.2, or 10 mg Cu-Zn/m^3 for 13 weeks, followed by a 4-week recovery period. Rats were exposed nose-only to aerosols with average mass median aerodynamic diameters of 1.1 μm (geometric standard deviation 2.7). The Cu-Zn alloy did not accumulate in lungs, indicating that it cleared rapidly and reached equilibrium concentrations in tissues of the respiratory tract after a few days of exposure. The 13-week exposures produced adverse biological changes only in the respiratory tract. Focal atrophy (mild severity) of olfactory epithelium occurred in 14 percent of the rats exposed to 1.0 or 3.2 mg Cu-Zn/m^3, and in 68 percent of rats exposed to 10 mg Cu-Zn/m^3. This lesion resolved during the recovery period in rats exposed to 1.0 mg Cu-Zn/m^3, but was still present in 2 percent and 32 percent, respectively, of the rats exposed to 3.2 or 10 mg Cu-Zn/m^3. A mild alveolar macrophage hyperplasia occurred in 50 percent of the rats exposed to 3.2 mg Cu-Zn/m^3, and a mild to moderate macrophage hyperplasia occurred in 82 percent of the rats exposed to 10 mg Cu-Zn/m^3. After the recovery

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19. ABSTRACT (Cont.) period, macrophage hyperplasia (mild severity) persisted in 23 percent of the rats exposed to 3.2 mg Cu-Zn/m^3 and in all of the rats exposed to 10 mg Cu-Zn/m^3. A mild type II pneumonocyte hyperplasia occurred in 27 percent of rats exposed to 3.2 mg Cu-Zn/m^3, and a mild to moderate hyperplasia occurred in 77 percent of rats exposed to 10 mg Cu-Zn/m^3. Recovery from type II pneumocyte hyperplasia was comparable to that observed for alveolar macrophage hyperplasia. Mild alveolitis was produced in 25 percent of the rats exposed to 3.2 mg Cu-Zn/m^3, and mild to moderately severe alveolitis was produced in 82 percent of the rats exposed to 10 mg Cu-Zn/m^3. Alveolitis resolved during the 4-week recovery period. After exposure to 10 mg Cu-Zn/m^3, changes in bronchoalveolar lavage fluid (BALF) constituents corresponded closely to the histological changes. Changes in BALF included increased total cells, macrophages, neutrophils, lymphocytes, collagenous peptides, and beta-glucuronidase. The only significant changes produced in BALF by exposures to 3.2 mg Cu-Zn/m^3 were (1) increased numbers of neutrophils, and (2) an increase in alkaline phosphatase that was not seen in rats exposed to 10 mg Cu-Zn/m^3. These changes in BALF were all relatively small and represented a mild inflammatory response that resolved during the recovery period. Exposures to 3.2 or 10 mg Cu-Zn/m^3 resulted in increased numbers of lymphoid cells in lung-associated lymph nodes. Although the number of antibody-forming cells/million lymphocytes was significantly depressed after recovery from exposures to 3.2 and 10 mg Cu-Zn/m^3, the total number of antibody-forming cells was not different from what was observed in sham-exposed rats. The only effect of inhaled Cu-Zn on respiratory function was reduced carbon monoxide diffusing capacity, produced by exposure to 10 mg Cu-Zn/m^3. This suggested responses to the inhaled Cu-Zn resulted in impaired alveolar-capillary gas exchange at the membrane level. The magnitude of this functional change was small. In summary, exposures to 3.2 or 10 mg Cu-Zn/m^3, 1.5 hours/day, 4 days/week for 13 weeks produced significant lesions and functional changes in the respiratory tracts of F344/N rats. The only lesion produced by exposure to 1.0 mg Cu-Zn/m^3 was a mild focal atrophy of olfactory epithelium in 14 percent of the rats; this lesion resolved within 4 weeks after exposure to Cu-Zn ended. No effects were detected after exposure to 0.32 mg Cu-Zn/m^3. Considering the cumulative results of this study, the no observable adverse effects level (NOAEL) for exposures of F344/N rats is defined as exposures equivalent to inhalation of 0.32 mg Cu-Zn/m^3, 1.5 hours/day, 4 days/week.

A-1

I. EXECUTIVE SUMMARY

The U. S. Army Biomedical Research and Development Laboratory (USABRDL) sponsored the Lovelace Inhalation Toxicology Research Institute (LITRI) to study the inhalation toxicity of respirable aerosols of powdered Cu-Zn alloy (Cu-Zn). Toxicological information was limited for this material and the LITRI responded to the need for information by studying the inhalation toxicity of this material in F344 rats.

Studies of the inhalation toxicity of Cu-Zn were conducted in three phases. Phase I included (1) standardization of methods for generation and delivery of aerosols of test materials, (2) physical/chemical characterization of the aerosols, (3) comparisons of nose-only versus whole-body exposure systems, (4) an assessment of stress imposed on the rats during nose-only versus whole-body exposure to 100 mg Cu-Zn/m3, and (5) preliminary evaluations of toxicity of inhaled Cu-Zn. Phase II consisted of repeated intermittent exposures to determine subacute toxic effects from exposure to different aerosol concentrations of the Cu-Zn. In Phase III, a 13-week subchronic exposure of rats to selected levels of Cu-Zn was used to determine a no observable adverse effects level (NOAEL) of exposure and estimate the reversibility of any toxic lesions. This report is for Phase III studies.

F344/N rats were exposed by inhalation in nose-only exposure tubes. Exposures were 1.5 hours per day, four days per week, for 13 weeks. Aerosol concentrations of Cu-Zn were 0 (sham), 0.32, 1.0, 3.2, or 10 mg Cu-Zn/m^3. The aerosols had average mass median aerodynamic diameters of 1.1 μm and geometric standard deviations of 2.7. Rats were weighed twice weekly during the 13-week exposure series. Pulmonary function evaluations were made before starting the exposures, midway through the exposure series, after the last exposure, and again after a 4-week recovery period. Additional evaluations were made after the exposure series and again after a 4-week recovery period to determine the

kinds and magnitudes of biological responses to the inhaled Cu-Zn alloy. The evaluations quantitated indicators of biochemical and cytological changes in bronchoalveolar lavage fluid (BALF), immunologic responses, phagocytic ability of pulmonary alveolar macrophages, collagen content of lung, and histopathological changes in the respiratory tract. Table ES-1 contains a summary of significant adverse effects observed in Phase III.

No rats died during the exposures as a result of inhalation of the test material. Body weight, an indicator of morbidity or toxicity, was decreased in rats exposed to 10 mg Cu-Zn/m^3. A change in pulmonary function was noted at the end of exposure only in rats exposed to 10 mg Cu-Zn/m^3. Rats in this group had decreased carbon monoxide diffusing capacity that did not completely resolve during the 4-week recovery period. Exposures to 3.2 and 10 mg Cu-Zn/m^3 produced changes in biochemical/cytological indicators of toxicity in bronchoalveolar lavage fluid (BALF). Specifically, β-glucuronidase and protein increased. Alkaline phosphatase increased in rats exposed to 3.2 mg Cu-Zn/m^3, but not in rats exposed to 10 mg Cu-Zn/m^3. Lactate dehydrogenase in BALF was not different from values for sham-exposed rats. These changes were resolved during the 4-week recovery period. Exposures to 3.2 or 10 mg Cu-Zn/m^3 caused increased numbers of lymphoid cells in lung-associated lymph nodes, and exposure to 10 mg Cu-Zn/m^3 significantly increased the total number of antibody-forming cells. These changes resolved during the 4-week recovery period. The concentration of antibody-forming cells in these lymph nodes was normal at the end of exposure in all groups of rats, but was depressed after the 4-week recovery period in rats exposed to 3.2 or 10 mg Cu-Zn/m^3. Exposure to 10 mg Cu-Zn/m^3 resulted in decreased phagocytic ability of pulmonary alveolar macrophages. No significant changes in pulmonary function, immunology, or phagocytic ability of macrophages resulted from the exposures to 0.32 or 1.0 mg Cu-Zn/m^3.

Table ES-1

Summary of Significant Adverse Effects Observed in Phase III

	Aerosol Concentration of Powdered Cu-Zn Alloy					
	1.0 mg/m^3		3.2 mg/m^3		10 mg/m^3	
Measure	EOE[a]	REC	EOE	REC	EOE	REC
Body Weights					D[b]	
Bronchoalveolar Lavage Fluid Analyses						
Total Cells					I	
Neutrophils			I		I	
Lymphocytes					I	
Macrophages					I	
Beta-Glucuronidase					I	
Alkaline Phosphatase			I			
Collagenous Peptides					I	
Immunology, Lung-Associated Lymph Nodes						
Total Lymphoid Cells			I		I	
Antibody-Forming Cells per Million Lymphocytes				D		D
Total Antibody-Forming Cells					I	
Macrophage Phagocytosis					D	
Respiratory Function						
Carbon Monoxide Diffusing Capacity					D	D
Histopathology[c]						
Lung Weights					I	
Nasal Epithelial Atrophy	3/22 (1.0)		6/44 (1.0)	1/43 (1.0)	15/22 (1.2)	7/22 (1.1)
Alveolar Macrophage Hyperplasia			24/44 (1.0)	10/43 (1.0)	18/22 (1.4)	22/22 (1.0)
Type II Pneumocyte Hyperplasia			12/44 (1.0)	8/43 (1.0)	17/22 (1.2)	22/22 (1.0)
Alveolitis			11/44 (1.0)	1/43 (1.0)	18/22 (1.4)	0/22

[a]EOE signifies measurements after the 13-week exposure; REC signifies measurements after the 4-week recovery period.

[b]There was a statistically significant ($p < 0.05$) increase (I) or decrease (D) in these measures, as compared with the sham-exposed rats.

[c]Only the data for lung weight are presented on the basis of statistical differences. Data for the respiratory tract lesions represent frequency of lesions, (number of rats with lesion)/(number of rats observed), and the average severity of the lesions for rats that had lesions. Average severity scores of 1.0 to 1.4 in this table indicate slight to moderate severity.

The Cu-Zn did not accumulate in lungs during the 13 weeks of exposure, indicating that it cleared rapidly. This suggests that an equilibrium concentration of the material in the respiratory tract was reached within days after the start of the 13-week subchronic exposure.

Histopathological lesions were limited to nasal airways and the pulmonary region of the respiratory tract. The nasal airways contained lesions after inhalation of 1.0, 3.2 and 10 mg Cu-Zn/m^3 for 13 weeks. Focal atrophy (mild severity) of the olfactory epithelium occurred in 15 of 22 rats exposed to 10 mg Cu-Zn/m^3, in 6 of 44 rats exposed to 3.2 mg Cu-Zn/m^3 and in 3 of 22 rats exposed to 1.0 mg Cu-Zn/m^3. After the recovery period, this lesion in the nasal airways persisted in 7 of 22 rats exposed to 10 mg Cu-Zn/m^3 and in 1 of 43 rats exposed to 3.2 mg Cu-Zn/m^3. It was not present after the recovery period in rats exposed to 1.0 mg Cu-Zn/m^3.

Lung weights were increased at the end of exposure in rats exposed to 10 mg Cu-Zn/m^3, but were normal after the recovery period. Multifocal type II pneumocyte hyperplasia, alveolitis, and alveolar macrophage hyperplasia were the principal alterations found in the lungs. All three types of lesions (mild severity) were produced in rats exposed to 3.2 and 10 mg Cu-Zn/m^3, but not in rats exposed to 0.32 or 1.0 mg Cu-Zn/m^3. The alveolar macrophage hyperplasia and type II pneumocyte hyperplasia persisted, but the alveolitis resolved during the 4-week recovery period.

No lesions occurred in rats exposed for 13 weeks to 0.32 mg Cu-Zn/m^3, and the nasal epithelial atrophy observed after exposure to 1.0 mg Cu-Zn/m^3 resolved during the 4-week recovery period. We conclude that the no observable adverse effects level (NOAEL) for exposure of F344/N rats to Cu-Zn alloy powder is equivalent to daily inhalation exposures of 0.32 mg Cu-Zn/m^3 for 1.5 hours per day, 4 days/week.

II. FOREWORD

Citations of commercial organizations and trade names in this report do not constitute an official Department of the Army endorsement or approval of the products or services of these organizations.

In conducting the research described in this report, the investigator(s) adhered to the "Guide for the Care and Use of Laboratory Animals," prepared by the Committee on Care and Use of Laboratory Animals of the Institute of Laboratory Animal Resources Commission of Life Sciences, National Research Council (NIH Publication No. 85-23, Revised 1985).

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V. EXPERIMENTAL METHODS

A. Test Material

We obtained Atlantic Brass Richgold fine 1800 from Atlantic Powdered Metals, Inc., New York, NY. This powdered metal alloy was from lot number T-7464. We mixed the bulk material in a plastic-lined 55 gallon drum, then transferred part of the powder to 9 approximately 2-liter sub-lots in Teflon bottles for convenience of storage and use. The remainder of the bulk material was returned to its shipping containers. This metal powder contained approximately 2/3 Cu and 1/3 Zn by weight. In Phase I of this project we determined the projected area diameter of bulk and aerosolized powder. Results indicated that most of the particles in this powder were flakes, having projectec area diameters in the range 0.6 to 16.4 mm. We also estimated the thickness of the flakes to be one-thirtieth to one-fourtieth of the projected area diameter. Aerosols generated using this powder typically had mass median aerodynamic diameters of approximately 0.9 to 1.2 mm, with geometric standard deviations in the range of 3.1 to 3.5.

B. Experimental Design for Phase III

Fischer-344/N rats were used in this study to allow comparisons with specific results from other related studies and to make general comparisons with the growing inhalation toxicology data base for rats. This laboratory animal species was suitable for pulmonary function evaluations during and after exposure to the test material, and procedures for evaluating specific endpoints have been well defined for rats.

Rats were 17 weeks old at the start of their exposures. The rats were weighed during the week prior to exposure and those body weights were used to randomize them for assignment to their study groups. The

randomization procedure made use of the LITRI Path/Tox Data System (Xybion Medical Systems, Inc., Cedar Knolls, NJ) and RS/1 Computer Software (BBN Software Products Corporation, Cambridge, MA). The result of the randomization procedure was assignment of rats to the experimental groups as indicated in Table 1.

The study was conducted in two parts because of a technical problem that caused the death of the sham-exposed rats in Phase III, Part 1. Preliminary results were available from Phase III, Part 1 at the time Phase III, Part 2 was planned. On the basis of the preliminary results, exposures to 10 mg Cu-Zn/m^3 and some of the endpoint evaluations were not repeated in Phase III, Part 2. However, one additional exposure group was included in Phase III, Part 2, to extend the lowest exposure concentration to 0.32 mg Cu-Zn/m^3.

Exposures were nose-only and target aerosol concentrations were 0, 0.32, 1.0, 3.2, and 10 mg Cu-Zn/m^3. Exposure durations were 1.5 hr/day, exposure frequencies were 4 times per week (usually Monday thru Thursday), and the exposure series was continued for 13 weeks, followed by a recovery period of 4 weeks. Sham-exposed rats are referred to as "shams", and were exposed 1.5 hr/day, 4 times per week to filtered air.

Previous observations in Phases I and II (Snipes et al., 1986, 1988) of this project and by others (Thomson et al., 1986) indicated that the most likely responses in Phase III would involve the nasopharynx and pulmonary region of the respiratory tract. Observations and endpoints of interest therefore emphasized the respiratory tract.

The lung is a primary route of entry into the body for airborne materials. Some inhaled materials cause responses in the lung which can be

Table 1

Exposure Groups of F344/N Rats for Phase III, Parts 1 and 2[a]

Target mg Cu-Zn/m^3	Part 1 Experiment Number	Part 1 Number of Animals	Part 2 Experiment Number	Part 2 Number of Animals
0 (sham)	b		4442	76
0.32			4443	44
1.0	4371	76		
3.2	4372	76	4444	76
10	4373	76		

[a]Exposures 1.5 hours/day, 4 days/week, for 13 weeks; equal numbers of males and females.

[b]Animals died due to technical problem during exposure.

measured by changes in composition of the lung tissue or by changes in the fluids and cells lining the bronchoalveolar airways. Since fibrosis of the lung was a possible response to the inhaled Cu-Zn, the lung tissue was analyzed for indications of developing fibrosis. Analysis of bronchoalveolar lavage fluid was used to detect an inflammatory response in the lung. This method has proven useful in previous studies on the toxicity of inhaled mineral dusts, coal combustion fly ash, and other toxicants (Beck et al., 1981, 1982; Henderson et al., 1978a, 1978b, 1979a, 1979b; Moores et al., 1980, 1981).

The measurements and endpoints (Table 2) included in Phase III of this project were selected to determine changes in important indicators of general health, the respiratory tract, or specific organ functions as a consequence of the exposures. Rats were observed daily and their body weights were recorded twice weekly during the 13-week exposure period.

Rats were randomly assigned for evaluations and for whether they would be evaluated at the end of the exposure or after the 4-week recovery period. The first groups of rats were killed three days after their last exposure to the Cu-Zn, the rest were killed 4 weeks later. The exceptions to this sacrifice schedule were the rats used for pulmonary function evaluations. Pulmonary function measurements were made prior to starting the exposures, midway through the 13 week exposure series, after the last exposure, and again after the 4-week recovery period.

C. Animals: Source, Identification and Housing

Rats were obtained from Charles River Laboratories, Kingston, NY. They were shipped from a viral-antibody-free facility in filter crates and were 13 weeks old when they arrived at the LITRI. Prior to the animals'

Table 2

Summary of Biological Evaluations Scheduled for Phase III, Parts 1 and 2

Endpoint Category	Part 1	Part 2[a]
Lavage Fluid Analyses	X	X
Clinical Chemistry	X	
Connective Tissue	X	X
Hematology	X	
Histopathology	X	X
Immunology	X	X
Lung Burdens of Cu and Zn	X	
Phagocytosis	X	X
Pulmonary Function	X	X

[a]Evaluations were limited to sham-exposed rats and rats exposed to 3.2 mg Cu-Zn/m^3 for all categories other than histopathology. All groups were evaluated for the presence of histological lesions.

arrival, the room selected for their housing was disinfected. This was accomplished by sponging or mopping all surfaces of the room with diluted Johnson's Expose (National Sanitary Supply Co., Albuquerque, NM), then fumigating the room with AN-FA-CIDE-S® (Pharmaceutical Research Laboratories, Greenwich, CT). Thereafter, quarantine procedures were followed for personnel, food, cages, bedding, and equipment taken into the room. Personnel donned shoe covers, clean laboratory coveralls, hair covers, and respiratory protection as they entered the room. All work was done while wearing disposable rubber gloves. Food, cages, and bedding were sterilized prior to placement in the room. Any equipment, such as analytical balances, was disinfected prior to placing it in the room. Access to the room was restricted to the limited number of personnel required for animal maintenance and handling animals for exposures. The rats were maintained under these quarantine conditions throughout the study.

All animals assigned to the project had unique individual identification numbers. The numbers were affixed to the animals' ears in the form of permanent metal ear tags. Ear tags were attached during the week before inhalation exposures were started. Missing ear tags were replaced as necessary to maintain positive identification of each animal.

Rats were housed two or three per cage in polycarbonate cages 20 cm H x 25 cm W x 45 cm L. Cages had polyester filter caps to reduce possible spread of disease and parasites. Cages and filter caps for the sham group were kept separate from cages and filter caps used for the rats exposed to the Cu-Zn. Also, the cages used for this study were not mixed with similar cages being used in the same housing area for other studies. Normal cage washing procedures were used, but control and exposed cages were washed separately from each other and from other cages in the building.

Cages had hardwood chip bedding which was changed twice weekly. Certified Rodent Blox pellets (Allied Mills, Chicago, IL) and water were available *ad libitum* in the housing area. Food was analyzed by the Continental Grain Company, Libertyville, IL. Data sheets from analysis of Lot P07236-1 of this feed by the Continental Grain Company are included in the Appendix. This analysis was representative of the feed used during Phase III, Parts 1 and 2.

Light was provided on a 12-hour daily cycle (0600-1800). Room temperature was maintained at 20 to 24 C, and relative humidity was 30 to 50 percent.

D. Animal Surveillance

The rats for Phase III, Parts 1 and 2 were 13 weeks old when they arrived at the Institute. They were placed directly into a quarantine room where they were maintained throughout the study. Their exposures to Cu-Zn started when they were 17 weeks old. The surveillance procedures described below were the same for rats in Phase III, Parts 1 and 2.

Within 48 hours of arrival at ITRI, 5 male and 5 female rats were examined for pinworm ova by the cellophane tape preparation method. All rats were negative for pinworm ova.

Prior to beginning exposures, 5 male and 5 female rats were killed for disease surveillance, which included gross necropsy, parasitology screening, and serology. Samples of the serum were sent to Microbiological Associates, Inc. (Bethesda, MD) for serologic testing for the following diseases: pneumonia virus of mice (PVM), kilham rat virus (KRV), Toolan's H-1 virus (H-1), sendai virus, rat coronavirus-sialodacryoadeniti virus (RCV-SDA), lymphocytic choriomeningitis virus (LCM), reovirus type 3 (Reo3), mouse

adenovirus (MAD), GDVII, and *Mycoplasma pulmonis*. A cellophane tape preparation was also done on each of the 10 rats to examine for pinworm ova (*Syphacia muris*). Fecal samples from 5 males and 5 females were submitted for fecal flotation analysis.

No gross lesions were observed in any of the rats. All rats were negative for parasites on fecal flotation and cellophane tape preparations. On serology, all rats were negative for antibodies to *Mycoplasma* and all viruses tested.

Periodically throughout the study, 10 sentinel animals (5 male, 5 female) from Phase III, Part 1 and Phase III, Part 2 were tested for pinworm ova via the anal tape technique. All sentinel rats tested negative for pinworms prior to the conclusion of the study. At the conclusion of the study, the sentinel rats were subjected to the disease surveillance procedures described above. No gross lesions were observed, and all rats were serologically negative for *Mycoplasma* and all viruses tested. The majority of sentinel rats were positive for ova of *Syphacia muris* at this final sacrifice.

E. Aerosol Generation and Exposure Systems

1. Aerosol Generation and Delivery Systems

One requirement for this project was to minimize changes in physical and chemical characteristics of the powdered Cu-Zn alloy. This required using an aerosol generator which would not grind or otherwise alter the size and shape of the powder. In addition, a suspension of the powder was not possible, since this would require a solvent which might alter the test material physically or alter the exposure patterns for the rats. Testing in Phase I (Snipes *et al*., 1986) of this project indicated that the Model 0101-C6S Jet-O-Mizer aerosol generator (Fluid Energy Corp., Hatfield, PA)

would be appropriate for this study. The Jet-O-Mizer, with its Accurate bulk materials feeder produced aerosols of the Cu-Zn having the desired exposure concentrations, stability, and volume production.

In all cases where aerosols of the Cu-Zn were used, the aerosol generation systems were enclosed to protect the operator(s) from exposure. These enclosures were made of 1.3 cm thick plexiglass and were equipped with glove ports and pass boxes. The enclosures were maintained at a relative negative internal pressure of 0.5-0.75 inches (1.3-1.9 cm) of hydrostatic pressure. This ensured that any leaks in the system would result in room air being drawn into the enclosure rather than test material escaping from the enclosure to contaminate the work environment and result in personnel exposures.

Each daily operation of this aerosol generation system started with a fresh supply of bulk Cu-Zn. The bulk powder was stored in 2-liter Teflon containers. Containers were physically mixed by turning them end over end 25 times prior to transfer of the bulk material. This procedure was done to obviate daily variations in aerosols due to differential settling of particles in the storage containers.

Aerosols were produced by the Jet-O-Mizer aerosol generation system using filtered air that was humidified to maintain relative humidity in the range 30 to 50 percent. Aerosols were passed through the exposure chambers or through a bypass as excess aerosol. Excess aerosol flow was drawn through a high efficiency particulate air (HEPA) filter via the exposure chamber exhaust system; the exposure chambers were exhausted through a separate HEPA filtered vacuum exhaust system.

2. Animal Exposure Chambers

Three 96-port nose-only exposure chambers were used for exposing rats to the Cu-Zn; an 80-port nose-only chamber was used to expose the shams. These multiport small animal exposure systems were similar to those described by Raabe et al. (1973). During exposures, rats were in polycarbonate nose-only exposure tubes. These tubes were designed to allow inhalation exposures of rats, while minimizing external contamination of the animals. The wall thickness of the Lexan tubes was 2.3 mm and the tube diameter was adequate to restrain the rats, but allow them space for thoracic expansion during breathing. The front end of each tube was tapered internally to conform to the shape of the rat's head and the rear end of the tube was closed by an adjustable plunger. The rats were secured in these tubes during exposure, with their noses projecting slightly past the end of the exposure tube and into the aerosol passing through the exposure chamber.

3. Aerosol Physical Characterization

Three types of aerosol samples were collected. Filter samples were collected to determine aerosol concentrations, Lovelace Multijet (LMJ) cascade impactors were used to collect samples for aerosol size determinations, and point-to-plane electrostatic precipitator (ESP) samples were collected for routine aerosol morphology evaluations.

A RAM-S real-time aerosol monitor (GCA Corporation, Bedford, MA) was used to continuously monitor the aerosol concentrations during testing and exposures. The primary use of this monitoring device was to provide real-time indications of the functional state of the aerosol generation and delivery systems. This information was used by the exposure technician to make any necessary adjustments within the systems to maintain the desired exposure conditions.

4. Exposure Chamber Aerosol Distribution Evaluations

The following procedures were used to quantitate uniformity of aerosol generator output and aerosol concentration within the exposure chambers. Three nose-only exposure systems were used for Cu-Zn and all three systems required testing prior to animal exposures. One system (10 mg Cu-Zn/m^3) had been used in Phase II of this project (Snipes et al., 1988) and testing for that chamber was not repeated prior to starting exposures for Phase III, Part 1. Chambers designated for producing aerosols and exposing rats to 0.32, 1.0, and 3.2 mg Cu-Zn/m^3 were tested prior to inhalation exposures of rats. Tests of generator output, stability, and uniformity of chamber distribution of the aerosols of Cu-Zn were conducted four hours per day, on three separate days with no animals in the exposure chambers. Previously identified exposure ports (Snipes et al., 1988) were sampled simultaneously to evaluate the aerosol concentration at each port. The amounts of test material were determined by weighing the filters before and after the aerosol collection intervals. Twelve simultaneous filter samples were collected, six from each side of each exposure chamber. Aerosols were collected on these filters for 40 minutes with 1 liter/minute sampling flow rates. A total of 144 samples were collected for each nose-only exposure chamber and used in the evaluation of spatial and temporal distribution patterns for the test aerosols of Cu-Zn. Lovelace Multijet impactor samples were also collected during these daily tests for aerosol size determinations.

F. Animal Exposure Procedures

It had been determined that the aerosols were almost uniformly distributed in the nose-only chambers. However, to minimize variability, a randomization procedure was used to assign each rat to its exposure location

for each exposure. A different list of exposure locations was produced for each group of rats, for every exposure. The procedure used computer software which randomized the list of rats to be exposed in each chamber and overlaid the random list of rats on the list of exposure ports available. Exposure ports were identified by a 3-digit code where each port of an exposure chamber was assigned a unique number. The procedure not only randomly assigned the rats to their exposure locations each day, the computer output file was used to generate labels which were placed on the exposure tubes at the time the rats were loaded into them. The labels facilitated accounting for each rat and reduced errors associated with handling rats for nose-only exposures and returning them to their assigned housing cages. The exposure location history for each rat in the study is in a master computer file for examination if needed.

The animals were housed in a room almost directly across a hallway from the exposure room. On exposure days, the rats were loaded into their polycarbonate exposure tubes in their housing room and transported to the exposure room in the exposure tubes. Animals to be sham-exposed were always handled and transported first. After the nose-only exposures, the rats were transported back to the housing room in the exposure tubes, and were unloaded from the tubes directly into their cages.

G. Aerosol Characterization During Animal Exposures

During the animal exposures, three types of aerosol samples were collected for each exposure. These included (1) the Lovelace Multijet (LMJ) impactor samples for determining aerodynamic size distributions of the aerosols, (2) filter samples for aerosol concentration determinations, and (3) a point-to-plane electrostatic (ESP) sample for electron microscope

observations. The flow rates were set at 16.4 liters/minute for impactors, 1 liter per minute for filter samplers, and 0.2 liters/minute for the ESP. One sample each of the LMJ and ESP were collected at the beginning and end of each exposure. Three or four filter samples were collected for the entire 1.5 hour exposures.

H. Biological Observations During and After Exposures

1. General

The rat housing area was inspected twice daily for dead or moribund rats. More thorough examinations occurred twice per week when all of the rats were weighed. Personnel handling rats for exposures recorded any unusual behavior, coat color, excretions, and overall general appearance, if the rats did not appear normal. Any dead or moribund rats were to be necropsied as "unscheduled deaths", as indicated in ITRI Protocols FY86-016 and FY87-009.

After their last scheduled exposure, the rats were returned to their housing as usual. Three days later, excluding the rats assigned for pulmonary function evaluations, immunology, and tissue analysis for Cu and Zn, rats to be used for biochemistry, hematology, phagocytosis, connective tissue, and histopathology analyses were transported to the LITRI necropsy facility. The rats were anesthetized with halothane, then exsanguinated by cardiac puncture. Halothane anesthesia was chosen because it resulted in the least change in baseline parameters used in a screening test for lung injury (Henderson and Lowrey, 1983). Blood was collected in syringes containing 100 units of heparin and used for hematology evaluations. Details of analytical procedures are presented below.

Rats used for immunology and evaluation of lung content of Cu and Zn were immunized 7 days prior to sacrifice. At their scheduled sacrifice time, they were anesthetized with CO_2, exsanguinated via the brachial artery, and the lungs and lymph nodes were removed for analysis as detailed below.

The same procedures were repeated four weeks later with the other rats assigned for these endpoint evaluations. Specific procedures are given below. Rats assigned to the pulmonary function evaluations were killed and discarded as biological waste after their final pulmonary function tests.

2. Lavage Fluid Biochemistry and Cytology

Evaluations were made in groups of rats killed at the end of the exposures and additional groups of rats killed after allowing 4 weeks for recovery. Rats were anesthetized with halothane and killed by exsanguination. The heart and lungs were removed en bloc. The left lung was isolated from the right lung and was used for evaluation of histopathology. The right lung of each rat was lavaged with physiological saline (2 washes of 4 mL each for females and 2 washes of 5 mL each for males). The two recovered lavage fluid washes from individual rats were combined and centrifuged at 1000 x g for 15 minutes to separate the cells from the supernatant fluid.

The supernatant was analyzed for lactate dehydrogenase (indicator of cell death), beta-glucuronidase (lysosomal enzyme indicating high phagocytic activity and/or lysis of phagocytic cells), alkaline phosphatase (measure of type II lung cell response), and protein content (indicator of damage to the alveolar/capillary barrier). The cells in the pellet were resuspended in physiological saline and evaluated using a Coulter counter (Coulter Electronics, Hialeah, FL). An aliquot of the cell suspension was processed using a cytocentrifuge and differential cell counts were made.

Total airway collagen was measured as an indicator of possible remodeling of lung structural protein (Pickrell et al., 1975). To measure airway collagen, lavage fluid collagenous peptides were measured. These are soluble hydroxyproline-containing compounds which have leaked into alveoli and small airways and are recovered from the lung by endobronchial saline lavage. They reflect turnover of the extracellular collagenous matrix.

An aliquot of the lavage fluid supernatant was hydrolyzed in 6 N HCl (sealed under N_2) for 16 to 18 hours at 110°C to convert proteins to their individual amino acids. The acid solution was evaporated to dryness, samples were resuspended in 0.001 N HCl, and a colorimetric procedure was used to quantitate the amount of hydroxyproline present (Grant, 1965). Right lungs were hydrolyzed using the same procedure as for the lavage fluid. The acid was evaporated, the material was resuspended in 0.001 N HCl, samples were decolorized with charcoal filtration, evaporated to dryness again, and finally suspended in 0.001 N HCl. Next, the samples were analyzed for hydroxyproline using the colorimetric assay procedure. The collagen content of the samples was calculated by multiplying the lavage fluid hydroxyproline content by 7.46 to convert to collagen content. This conversion is based on the fact that collagen is approximately 13 percent hydroxyproline by weight (Neuman and Logan, 1950).

Based on data available at the time total lung collagen analyses were done, the only exposed group of rats likely to be different from controls was the group exposed to 10 mg Cu-Zn/m^3. We therefore elected to evaluate total lung collagen in two steps, doing the second step only if necessary. The first step included analysis of selected groups of rats killed at the end of the 13-week exposure, and only sham-exposed rats and rats

exposed to 10 mg Cu-Zn/m^3 from the animals allowed the 4-week recovery period. One half of the control animals from the group killed at the end of exposure was pooled with one half of the control animals killed after the recovery period. This was done to provide controls for these analyses, and to have controls available for additional analyses if they would have been justified.

Total lung collagen was measured for rats killed at the end of exposure to 0, 3.2, and 10 mg Cu-Zn/m^3. This included rats from Phase III, Parts 1 and 2 that had been exposed to 3.2 mg Cu-Zn/m^3, which was the only exposure level common to Parts 1 and 2. The only exposed group in which rats were evaluated after the 4-week recovery period was the group exposed to 10 mg Cu-Zn/m^3.

Additional lungs would have been analyzed as a second step in these evaluations if justified on the basis of observing significant changes in lung collagen for rats exposed to 3.2 mg Cu-Zn/m^3. Results for collagen content of lung were normalized and presented as amount of collagen per gram control lung, and amount per kilogram body weight.

3. Hematology and Serum Chemistry

Limited clinical tests were selected on the basis of results from previous phases of this study to determine effects, if any, in the hematopoietic system, and in other organ systems of the rats. Hematological analyses were performed at the end of inhalation exposures and 4 weeks later using a Coulter Model S-550 Hematology Analyzer. The following parameters were measured:

Hematocrit

Hemoglobin concentration

Erythrocyte count

Erythrocyte indices

Mean corpuscular volume (MCV)

Mean corpuscular hemoglobin (MCH)

Mean corpuscular hemoglobin concentration (MCHC)

Leukocyte count, total and differential

Chemistry parameters were also measured at the end of inhalation exposures and 4 weeks later using a centrifugal analyzer (Multistat, Fisher Instrumentation Laboratories, Lexington, MA). The following serum parameters were measured:

Alkaline phosphatase

Serum glutamic pyruvic transaminase (alanine aminotransferase)

Blood urea nitrogen

Total bilirubin

Total protein

Albumin

4. Immunology

A portion of inhaled particulates translocate to the lung-associated lymph nodes which receive lymphatic drainage from the lung. The results of studies on the effects of inhaled particulates indicate that insoluble materials which reach the lung-associated lymph nodes are retained in these tissues with a long half-life, and that this exposure can alter the immune function of these lymphoid tissues (Bice et al., 1985, 1987). Therefore, the effects of inhaled Cu-Zn on immune response in the lung-associated lymph nodes was evaluated.

Immunization was by intratracheal instillation of antigen (Bice et al., 1979) seven days prior to killing the rats. The rats were anesthetized with halothane, and the trachea was intubated with a catheter. The placement of the catheter in the trachea was verified by ventilating the lungs after placement. Particulate antigen (sheep red blood cells) was instilled just above the bifurcation of the trachea. A total of 100 million red blood cells (SRBC) obtained from a single sheep were used for each rat.

The number of lymphoid cells producing IgM anti-SRBC antibody were determined in the lung-associated lymph nodes and the spleen by the Cunningham modification of the Jerne plaque assay (Cunningham and Szenberg, 1968). Evaluation of the number of anti-SRBC in the spleen after lung immunization was necessary to determine if exposure to the Cu-Zn altered the antigen-trapping capacity of the lung-associated lymph nodes. Instilled SRBC that leave the lung via the lymphatics are normally removed in the lung-associated lymph nodes. This antigen does not reach distant lymphoid tissues, since the number of antigen-forming cells in the spleen is not significantly elevated above background level (Bice et al., 1979).

Antibody-forming cell data were expressed as the number of IgM anti-SRBC antibody-forming cells per million lymphoid cells in the lung-associated lymph nodes or in the spleen. A statistical comparison of the level of immunity in control rats and in exposed rats was made. Results of past studies indicated that the data are log-normally distributed (Gottlieb, 1974). Therefore, a logarithmic transformation of the data was done and the transformed data were evaluated using an unpaired Student's t-test with a BMDP computer program (BMDP, 1979).

5. Phagocytosis

As described above, lavage fluid was centrifuged and the supernatant used for biochemical analyses. The free alveolar cell fraction (pellet from the centrifugation step) was used for evaluation of phagocytosis by pulmonary alveolar macrophages (PAM). Smears of the cytocentrifuge pellets were made to allow differential cell counts. Phagocytosis of SRBC by PAM from the pellets was tested with and without surface-bound antibody (Harmsen *et al*., 1980).

The SRBC used in the phagocytosis assay were sensitized by incubation with anti-SRBC antibody (EA). A one percent suspension of EA was added to the alveolar macrophages obtained by lung lavage and incubated at 37°C for 60 minutes to allow time for phagocytosis. The EA and alveolar macrophages were then centrifuged, and the pellet was resuspended in distilled water to lyse any EA not phagocytized. Slides were prepared from the resuspended cells, and the number of SRBC phagocytized by 100 alveolar macrophages was counted using oil immersion with light microscopy.

6. Respiratory Function Measurements

Tests included a spectrum of measured and calculated parameters, allowing evaluation of the different facets of respiratory function: ventilation, lung mechanics, gas distribution, and alveolar-capillary gas transfer. The tests included assays that are sensitive and used most commonly in humans.

Rats were intubated with tracheal catheters, 5.5 cm long x 1.78 mm I.D., fabricated from 14 gauge intravenous catheters (Cathlon IV, No, 4428, Jelco, Raritan, NJ) as previously described (Mauderly, 1977). The breathing port in the plethysmograph wall was a Luer fitting (No, 6161,

Popper, New York, NY) drilled to 2.5 mm I.D. The frequency response of the plethysmograph-respirator-tracheal catheter system was tested and found adequate to record forced expirations of rats. The phasing of flow, volume, and transpulmonary pressure (Ptp) signals was tested by oscillating volumes into and out of the plethysmograph; no significant phase lag was detected within the frequency range of spontaneous breathing, the only condition in which phasing is critical.

Respiratory function measurements were similar to those previously published (Harkema et al., 1982; Likens and Mauderly, 1982; Mauderly, 1982). Tests were conducted using a 1.4 L combination flow (volume displacement) and pressure (constant volume) plethysmograph. Flows were determined by measuring differential pressures (MP45 transducer, Validyne, Northridge, CA) across 6 layers of 400-mesh wire cloth covering a 1.3 cm hole in the plethysmograph wall. Volumes were calculated by integrating flow (Model 6 pulmonary mechanics analyzer, Buxco, Sharon, CT). In the pressure mode, used only for measurement of functional residual capacity, the hole was sealed and volume changes were measured as pressure changes, using the same transducer. The plethysmograph was heated by a resistance element and maintained at approximately 37°C.

Transpulmonary (Ptp) pressure was measured using transducers (P23ID, Gould, Hato Rey, Puerto Rico) connected to the external airway and to a 2.2 mm O.D. esophageal catheter by liquid-filled tubes. The transducer outputs were conditioned by a differential amplifier (Buxco), which produced outputs for both transpulmonary and airway pressures.

A positive-negative pressure respirator system was used to induce quasistatic and forced expiratory movements. Reservoirs (4.6 L)

maintained at +40 and -50 cm H_2O were connected to the airway by solenoid valves. Inspiratory and quasistatic expiratory flow rates were limited by needle valves to 5 and 3 mL/second, respectively.

Inspiration was stopped automatically at a Ptp of +30 cm H_2O. Forced expiration was induced by opening a valve having a 9.5 mm diameter orifice (V52DA3012, Skinner, New Britain, CT) without intentional flow restriction between the valve and the low pressure reservoir.

The measurement sequence was as follows The rats were anesthetized with halothane in air, intubated with the tracheal catheter, and placed prone in the plethysmograph. The esophageal catheter was inserted and adjusted to maximize the Ptp signal. Anesthetic depth was standardized by adjusting the halothane concentration to yield a respiratory frequency of 55 ± 5 breaths/minute. Respiratory frequency, tidal volume, minute volume, dynamic lung compliance, and total pulmonary resistance were measured during spontaneous breathing by the mechanics analyzer, averaged for 15-20 breaths by a data logger (DL-12, Buxco) and displayed on a teletype terminal. The measurement of dynamic lung mechanics by the mechanics analyzer was identical in principle to the method of Amdur and Mead (1958).

Prior to each subsequent test procedure, the rats were hyperventilated with a syringe to induce temporary apnea and to establish a uniform lung volume history. A quasistatic exhalation was performed by inflating the lungs to +30 cm H_2O Ptp, then slowly deflating the lungs until expiratory flow stopped. Volume and Ptp signals were recorded on a strip-chart recorder. The inspired volume was defined as inspiratory capacity, the expired volume as vital capacity, and the difference as the expiratory reserve volume. Quasistatic pressure-volume relationships were

analyzed by a microprocessor contained within the data logger, and results were displayed on a teletype terminal. Quasistatic lung compliance was measured as the chord compliance between the apneic lung volume and that volume +10 cm H_2O Ptp.

Functional residual capacity was measured using Boyle's Law (DuBois et al., 1956) by inducing apnea, blocking the breathing port, and measuring airway pressure and lung volume changes as breathing resumed. Residual volume was calculated by subtracting expiratory reserve volume from functional residual capacity, and total lung capacity was calculated by adding residual volume to vital capacity.

A forced expiration was induced by inflating the lungs to +30 cm H_2O Ptp and rapidly deflating the lung until expiratory flow stopped. The event was analyzed by a microprocessor contained within the data logger, and both the flow-volume curve and several calculated variables were displayed on a teletype terminal. These variables included forced vital capacity, peak expiratory flow rate, percent of forced vital capacity expired in 0.1 second, mean mid-expiratory flow rate, and the maximal expiratory flow rates at 10, 25, and 50 percent of forced vital capacity.

Diffusing capacity for CO was measured by a single-breath method (Ogilvie et al., 1957). The gas volume required to increase Ptp from functional residual capacity to 20 cm H_2O was determined, and that volume of test gas containing 0.4 percent CO and 0.5 percent Ne in air was injected into the lung with a syringe. After approximately six seconds, one-half the injected volume was withdrawn from the lung and the remainder (alveolar sample) was withdrawn into a second syringe. Gas concentrations in the alveolar gas sample were determined by gas chromatography (Carle Model 111).

A single-breath N_2 washout was performed as described above for quasistatic exhalation, except that the test was started by deflating the lungs to residual volume and the subsequent inflation was with O_2 instead of air. An X-Y plot of volume exhaled versus N_2 concentration (percent) of the expirate was constructed and analyzed to calculate the slope of Phase III, the alveolar plateau.

7. Necropsy and Histopathology

Eleven male and 11 female rats from each exposure group listed in Table 1 were evaluated at the end of the exposure series, and another 11 male and 11 female rats were evaluated after the 4-week recovery period. The rats were anesthetized with halothane and exsanguinated, as indicated above. Some of the rats were shared for several evaluations. For shared rats, after removal of the heart-lung bloc, the left lung and carcass were subjected to gross examination and sampling for histopathology. For other rats, the entire lung was available for gross and histopathology evaluations. Organs grossly examined, weighed, saved in fixative, and examined microscopically are listed in Table 3.

The lungs were instilled intratracheally with 10 percent neutral buffered formalin (NBF) to approximately their normal inspiratory volume. The nasal cavity was perfused with 1-3 mL of 10 percent NBF to remove air before immersion in additional fixative. The stomach was injected with 10 percent NBF and fixed for gross examination. The other tissues listed in Table 3 were fixed by immersion in 10 percent NBF.

After allowing adequate time for complete fixation, tissues were trimmed, embedded in paraffin, and sectioned at 5 microns with a microtome. The sections were mounted on glass slides, stained with

Table 3

Tissues and Organs Grossly Examined, Weighed, Saved in Fixative and Examined Microscopically in Phase III, Parts 1 and 2

		Routine Histology	
Tissue or Organ[a]	Weighed	Part 1	Part 2
Thymus		X	
Tracheobronchial Lymph Nodes		X	X
Spleen		X	
Femur		X	
Larynx		X	X
Nasal Cavity		X	X
Trachea		X	X
Lung	X	X	X
Heart		X	
Stomach		X	
Liver	X	X	
Kidneys	X	X	
Urinary Bladder		X	
Testes	X	X	
Ovaries	X	X	
Adrenals		X	
Thyroid		X	
Brain	X	X	
Lesions (if present)		X	X

[a]All grossly examined and fixed in 10% neutral buffered formalin.

hematoxylin and eosin, and examined for lesions. Comparisons were made among the exposure groups for presence of lesions, types of lesions, and their severity. Results are discussed below and details for individual rats are included in the Appendix.

I. Atomic Absorption Analyses for Cu and Zn

These analyses were done only for Phase III, Part 1. Lungs were individually dried for about 15 hours at ~ 120°C, then transferred to Teflon digestion vessels containing 3.0 mL of ultrapure concentrated HNO_3, 1.0 mL of ultrapure concentrated HCl, and 0.1 mL of ultrapure concentrated HF. Samples were next placed in a microwave oven, heated for 6 minutes, then cooled in an ice water bath. Cooled digestates were added to 5.0 mL of 5 percent boric acid and the solution diluted to 25 mL with 0.06 M citric acid. The diluted solutions were assayed for Cu and Zn by atomic absorption spectroscopy using an Instrumentation Laboratories IL 951 graphite furnace atomic absorption instrument. The limits of detection and quantitation (American Chemical Society Committee on Environmental Improvement, 1983), and average recoveries of standard Cu and Zn are shown in Table 4. Attempts to measure recovery of the metal powder added directly to animal tissues were not successful because of difficulty in quantitatively transferring small amounts of the Cu-Zn.

J. Statistical Comparisons

Body weight and respiratory function data were available for comparisons among groups of rats before exposures to Cu-Zn started and midway through the 13-week exposure series. Sham-exposed rats in Phase III, Part 1 were accidentally killed one day before their exposures were to end. Also, some of the endpoint evaluations in Phase III, Part 1 were not repeated in Phase III, Part 2. Therefore, some of the comparisons in Phase III, Part 1

Table 4

Quality Control Information for
Absorption Analyses in Phase III, Part 1

Evaluation	Cu	Zn
Reagent blank (n = 9)		
µg/mL, mean ± SD	0.009 ± 0.006	0.006 ± 0.003
Limit of Detection[a], µg/mL	0.028	0.015
Limit of Quantitation[b], µg/mL	0.072	0.035
Percent Recovery, Mean ± SE		
Cu - NBS393, n = 8	92 ± 3.9	100 ± 2.2
Zn - NBS728, n = 8		

[a]Limit of detection is defined as the mean value plus 3 times the standard deviation for the reagent blank.

[b]Limit of quantitation is defined as the mean plus 10 times the standard deviation for the reagent blank.

were of necessity made between groups of rats exposed to 3.2 or 10 mg Cu-Zn/m^3 and rats exposed to 1.0 mg Cu-Zn/m^3. These comparisons are indicated at the appropriate places in text. Results for rats exposed to 3.2 mg Cu-Zn/m^3 in Phase III, Parts 1 and 2 were statistically compared and the judgement was made that all data from Phase III, Parts 1 and 2 could be presented as one set (Appendix I) and data for rats exposed to 3.2 mg Cu-Zn/m^3 could be combined. Statistical comparisons were then possible between groups of rats exposed to 0.32, 1.0, 3.2, and 10 mg Cu-Zn/m^3 and the sham-exposed rats from Phase III, Part 2. Therefore, with the exception of the body weight and respiratory function results, the immediate family of comparisons was limited to (1) groups of rats exposed to 3.2 or 10 mg Cu-Zn/m^3 in Phase III, Part 1, compared with the group of rats exposed to 1.0 mg Cu-Zn/m^3, (2) comparisons between rats exposed to 3.2 mg Cu-Zn/m^3 in Phase III, Parts 1 and 2, and (3) data from all exposed groups from Phase III, Parts 1 and 2 combined where possible and comparisons made with the sham-exposed rats from Phase III, Part 2. Comparisons were made between sets of data collected at the end of exposure or collected after the recovery period. Comparisons were not made between results from end of exposure and after recovery.

Unless specified otherwise, comparisons presented in this report included analysis of variance to detect overall group differences in mean and variance. Specific differences were measured using the Student's t-statistic with appropriate corrections for multiple comparisons according to the inequality of Bonferroni. We used the Levene test for equal variance to determine if we should use separate or pooled variance t values in our comparisons. If $p > 0.05$ for the Levene test, we used pooled variance values; for $p < 0.05$, we used the separate variance t.

VI. RESULTS

A. Exposure Aerosol Chamber Distribution Evaluations

In Phase III, Part 1, three aerosol concentrations of Cu-Zn were used (1.0, 3.2, and 10 mg Cu-Zn/m^3). In Phase III, Part 2, two aerosol concentrations were used (0.32 and 3.2 mg Cu-Zn/m^3). Temporal and spatial variation of aerosol concentrations was measured in each exposure system prior to exposures of animals. Results for the exposure system used to expose rats to 10 mg Cu-Zn/m^3 were obtained as part of Phase II of this project (Snipes et al., 1988). The other three aerosols were tested in Phase III, Part 1 (1.0 and 3.2 mg Cu-Zn/m^3) or Phase III, Part 2 (0.32 mg Cu-Zn/m^3).

Table 5 summarizes the results for tests of the temporal and spatial variation for the target concentrations of 0.32, 1.0, and 3.2 mg Cu-Zn/m^3. Temporal variation is the variation with time at a given position, and the spatial variation is the variation from location to location at a given time, or average over a given time period. The temporal variation was calculated from data for a given position from all test runs; the spatial variation was calculated from average concentrations of all sampling locations. The variation for the aerosol containing 0.32 mg Cu-Zn/m^3 was larger than for the other aerosols. This was anticipated since the lower concentration of particles in the aerosol dictated a greater degree of uncertainty in quantitating the aerosol. However, the coefficient of variation was less than the acceptable value of 20 to 25 percent. We conclude (1) that all aerosol concentrations were near the target levels, and (2) the aerosols for 3.2 mg Cu-Zn/m^3 were essentially identical for Phase III, Parts 1 and 2.

The aerosol size distributions as determined using the Lovelace Multijet cascade impactor during the chamber aerosol distribution evaluations

Table 5

Exposure Chamber Aerosol Distribution Evaluations Without Animals Present in Exposure Chamber[a]

Target Concentration of Cu-Zn Alloy Powder	Measurement	Phase III, Part 1	Phase III, Part 2
$0.32\ mg/m^3$	Temporal Variation	ND	7.9% ± 4.3%
	(Range)	ND	(1.5% - 14%)
	Spatial Variation	ND	7.6%
	Mean Concentration	ND	$0.31\ mg/m^3$
	Particle Size:		
	MMAD ± SD (μm)	ND	1.13 ± 0.17
	GSD ± SD	ND	3.41 ± 1.2
$1.0\ mg/m^3$	Temporal Variation	4.9% ± 0.7%	ND
	(Range)	(4.4% ± 5.4%)	ND
	Spatial Variation	5.1%	ND
	Mean Concentration	$0.97 \pm 0.05\ mg/m^3$	ND
	Particle Size:		
	MMAD ± SD (μm)	1.07 ± 0.045	ND
	GSD ± SD	3.00 ± 0.55	ND
$3.2\ mg/m^3$	Temporal Variation	2.5% ± 1.6%	2.6% ± 1.8%
	(Range)	(1.1% - 6.2%)	(0.9% - 5.9%)
	Spatial Variation	2.5%	0.9%
	Mean Concentration	$3.23\ mg/m^3$	$3.28\ mg/m^3$
	Particle Size:		
	MMAD ± SD (μm)	0.984 ± 0.064	0.982 ± 0.024
	GSD ± SD	2.51 ± 0.13	2.53 ± 0.058

[a]Aerosol distribution expressed as mean ± standard deviation (range) of the coefficient of variation for temporal variation, and as coefficient of variation for spatial variation.

ND = not done
MMAD = mass median aerodynamic diameter in μm
GSD = geometric standard deviation
SD = standard deviation

are also indicated in Table 5. These results were similar for all three aerosol concentrations and were comparable to those from Phase I (Snipes et al., 1986) and Phase II (Snipes et al., 1988) of this project, where we generated aerosols having 10, 40, and 100 mg Cu-Zn/m^3.

B. Aerosol Characterization During Animal Exposures

Figure 1 shows the mean weekly aerosol concentrations (± SD) for the three exposure chambers over the 13 week period of rat exposures. The overall mean aerosol concentrations were close to the target concentrations of 0.32, 1.0, 3.2, and 10 mg Cu-Zn/m^3 as shown in Table 6. The overall coefficient of variation was less than 15 percent. Also listed in Table 6 are the aerosol size distributions as determined by the LMJ cascade impactor samples during the 13 weeks of exposure. There were no significant size differences either among chambers or between exposure groups ($f = 2.49$; $p > 0.10$).

C. Biological Observations During and After Exposures

1. Animal Body Weights

Body weight results throughout the exposure period are summarized in Figure 2. The typical pattern for body weight was an initial drop during the first few days of the exposure series, followed by stabilization and gradual increase. Results for individual rats are in the Appendix.

Table 7 presents results for body weights taken at 5 selected times during the exposures. The only observed differences from sham-exposed rats occurred in rats exposed to 10 mg Cu-Zn/m^3. At the 13th week of exposure, the body weights for these rats (male and female) were statistically reduced, indicating a morbidity response associated with exposures to 10 mg Cu-Zn/m^3, 1.5 hours/day.

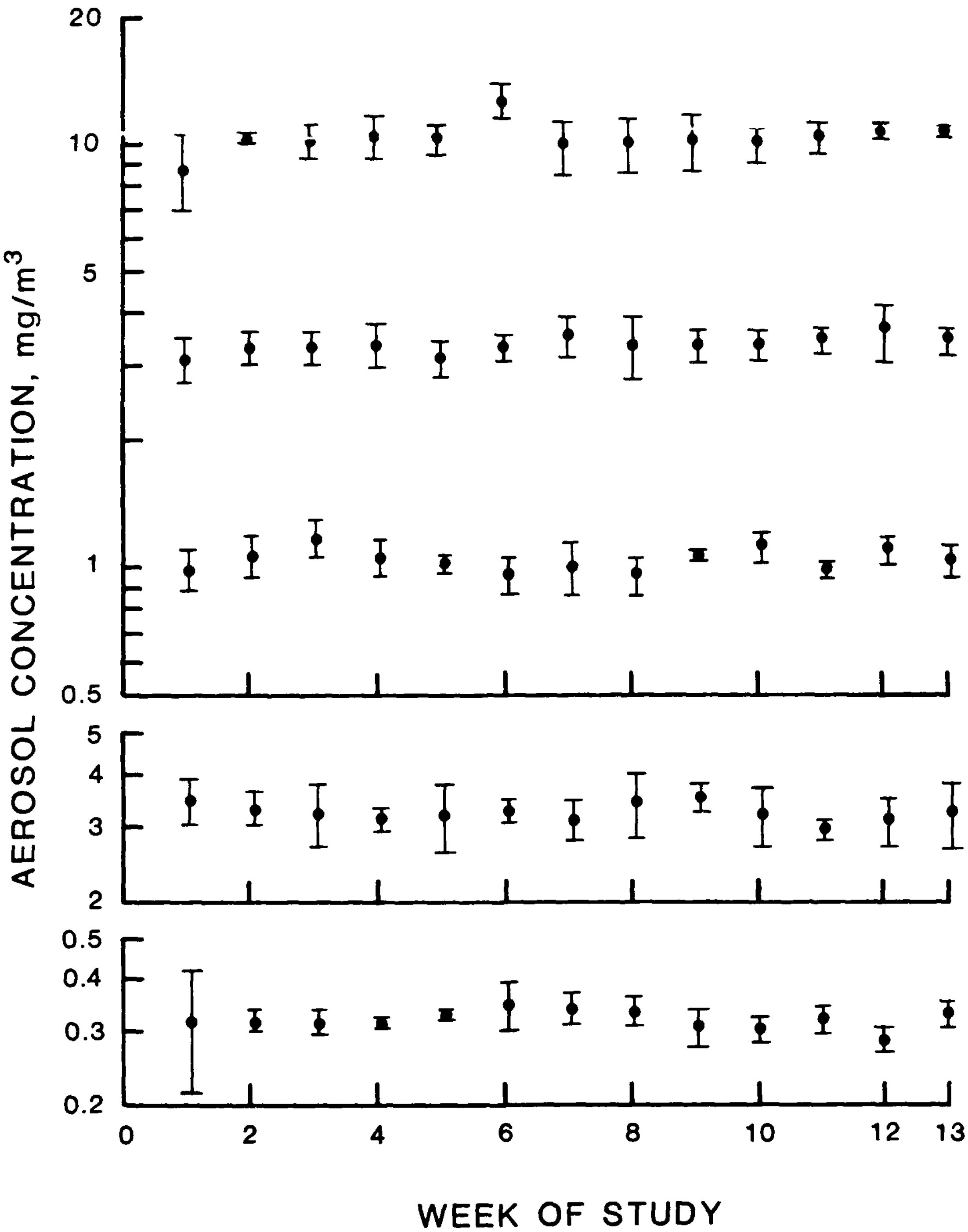

Figure 1. Aerosol concentrations (mean ± SD) of Cu-Zn alloy powder during 13 weeks of rat exposures in Phase III, Parts 1 and 2. The upper 3 sets of data were from Part 1, and the lower two sets of data were from Part 2. Individual values are in the Appendix.

Table 6

Summary of Cu-Zn Alloy Powder Exposure Atmosphere Concentrations and Size Distributions During 13 Weeks of Exposure for Phase III, Parts 1 and 2

Target Concentration of Cu-Zn Alloy Powder	Measurement	Phase III, Part 1	Phase III, Part 2
0.32 mg/m^3	Concentration, Mean ± SD	ND	0.318 ± 0.041
	Particle Size:		
	MMAD ± SD	ND	1.10 ± 0.16
	GSD ± SD	ND	2.43 ± 0.43
1.0 mg/m^3	Concentration, Mean ± SD	1.03 ± 0.11	ND
	Particle Size:		
	MMAD ± SD	0.99 ± 0.18	ND
	GSD ± SD	2.91 ± 0.44	ND
3.2 mg/m^3	Concentration, Mean ± SD	3.33 ± 0.33	3.24 ± 0.40
	Particle Size:		
	MMAD ± SD	1.00 ± 0.15	1.19 ± 0.14
	GSD ± SD	2.78 ± 0.37	2.67 ± 0.38
10.0 mg/m^3	Concentration, Mean ± SD	10.25 ± 1.30	ND
	Particle Size:		
	MMAD ± SD	1.09 ± 0.20	ND
	GSD ± SD	2.91 ± 0.36	ND

ND = not done

MMAD = mass median aerodynamic diameter in μm

GSD = geometric standard deviation

SD = standard deviation

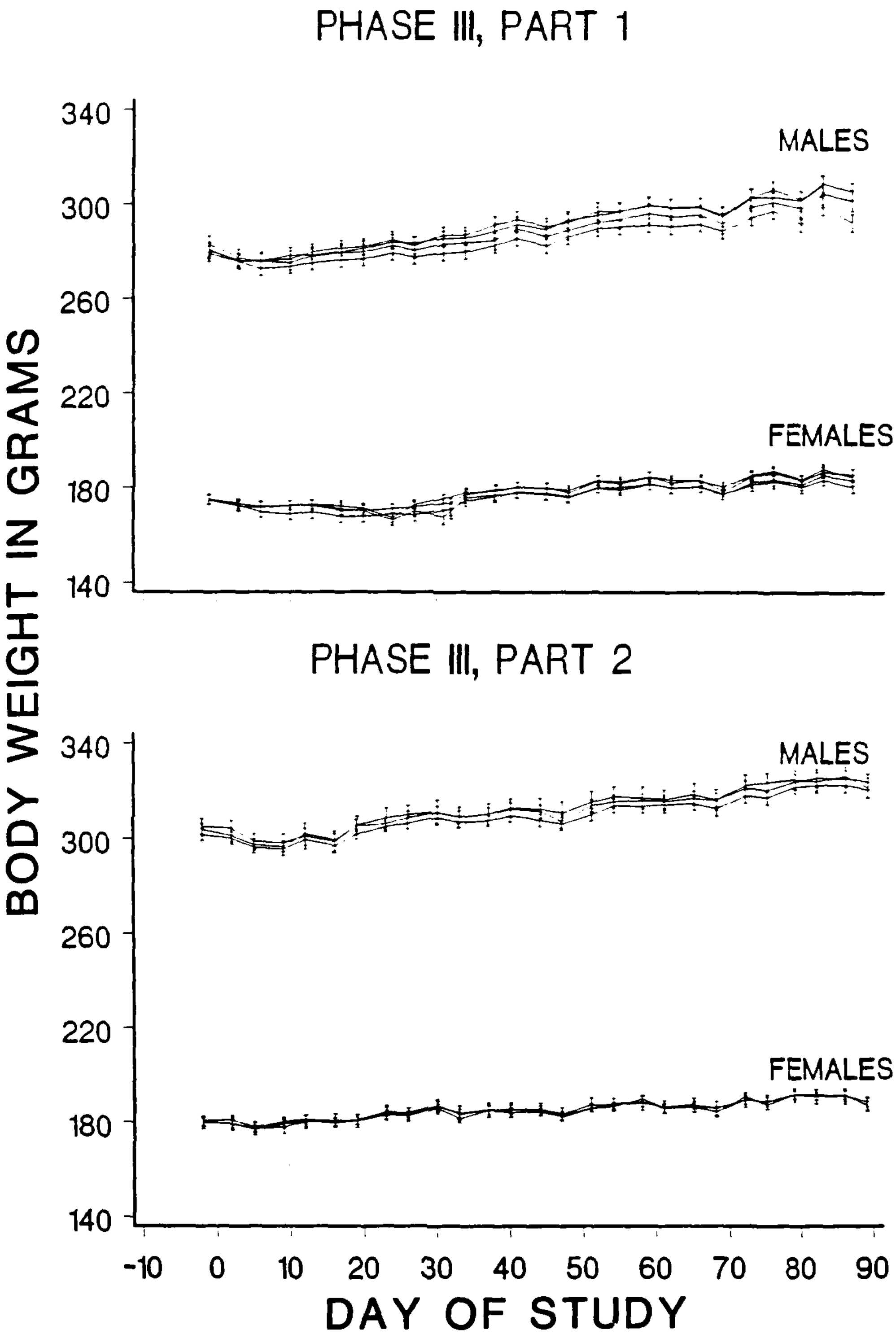

Figure 2. Body weights (mean ± SE) for rats in Phase III, Parts 1 and 2.

Table 7

Summary of Body Weights for Selected Times During 13 Weeks Exposure of F344/N Rats to Powdered Cu-Zn Alloy (Values are Mean ± SE)

			Day of Study Relative to First Exposure Day				
Part 1	mg Cu-Zn/m^3	N	-1	13	34	55	83
Females	0 (Sham)	36	174.9 ± 1.0	173.0 ± 0.9	177.9 ± 1.0	182.4 ± 1.0	188.0 ± 1.0
	1.0	36-38	174.8 ± 1.0	172.7 ± 1.1	175.9 ± 1.2	179.0 ± 1.1	185.4 ± 1.2
	3.2	38	175.2 ± 1.0	172.5 ± 1.0	177.2 ± 1.0	181.7 ± 1.0	186.8 ± 1.1
	10	38	175.1 ± 1.0	169.6 ± 1.4	174.5 ± 1.2	180.0 ± 1.1	183.5 ± 1.2[a]
Males	0 (Sham)	36	279.0 ± 1.6	279.7 ± 1.6	286.6 ± 1.7	296.7 ± 1.9	308.1 ± 1.9
	1.0	35-37	280.1 ± 1.6	277.9 ± 1.5	283.5 ± 1.8	293.4 ± 1.9	304.4 ± 2.3
	3.2	37-38	283.0 ± 1.7	278.2 ± 1.7	285.5 ± 1.5	296.7 ± 1.8	308.7 ± 1.9
	10	38	280.7 ± 1.5	275.1 ± 1.5	279.5 ± 1.5	290.2 ± 1.6	299.2 ± 2.0[b]

			Day of Study Relative to First Exposure Day				
Part 2	mg Cu-Zn/m^3	N	-2	12	33	54	86
Females	0 (Sham)	38	180.6 ± 1.0	181.2 ± 1.0	183.7 ± 1.0	187.9 ± 1.1	191.2 ± 1.1
	0.32	21-22	179.9 ± 1.4	180.3 ± 1.4	184.0 ± 1.5	187.5 ± 1.3	191.2 ± 1.6
	3.2	38	180.0 ± 0.9	180.5 ± 1.1	181.7 ± 0.9	186.8 ± 0.8	191.8 ± 0.9
Males	0 (Sham)	37-38	303.8 ± 1.2	301.9 ± 1.2	308.9 ± 1.3	315.4 ± 1.3	325.2 ± 1.8
	0.32	22	305.1 ± 1.6	301.0 ± 2.7	309.0 ± 2.1	317.6 ± 2.0	327.1 ± 2.1
	3.2	38	301.7 ± 1.2	299.5 ± 1.2	306.8 ± 1.2	313.8 ± 1.4	322.5 ± 1.5

[a]The treated groups were compared with the sham-exposed group using Student's t-test for unequal variances when Levene's test indicated the variances were not the same. When Levene's test did not show differences between the variances, Student's t-test for equal variances was used. Probability values were adjusted for multiple comparisons using Bonferroni's inequality; $p < 0.05$.

[b]$p < 0.01$.

2. Lavage Fluid Biochemistry and Cytology

As indicated in Tables 8 through 10, there was a definite inflammatory response in the highest level exposure group (10 mg Cu-Zn/m^3), for which the lavage fluid had increased total cells, macrophages, neutrophils, lymphocytes, protein, and beta-glucuronidase activity. There were also small, but significant increases in alkaline phosphatase in rats exposed to 3.2 mg Cu-Zn/m^3. These changes in alkaline phosphatase were questionable and did not appear to have biological significance, since there was no increase in alkaline phosphatase associated with exposures to 10 mg Cu-Zn/m^3.

It is important to note that all biochemical and cytological indicators of an inflammatory response had returned to normal by 4 weeks after the end of the exposure. This suggests an initial inflammatory response to the metal powder, followed by rapid clearance of the material from the lung and recovery from the inflammatory response.

3. Airway Collagenous Peptides and Total Lung Collagen

Table 11 shows the effects of 13 weeks of exposure, and exposure followed by a 4-week recovery period, on airway (lavage fluid) collagenous peptides. Rats exposed to 10 mg Cu-Zn/m^3 had increased airway collagen at the end of exposure, but not following 4 weeks recovery. No other exposures produced increased airway collagenous peptides at the end of exposure. Rats exposed to 1.0 mg Cu-Zn/m^3 had increased airway collagenous peptides following 4 weeks of recovery and the biological importance of this change was nil. Rats exposed to 0.32, 3.2, and 10 mg Cu-Zn/m^3 had airway collagenous peptide levels indistinguishable from those of sham-exposed rats after the recovery period.

Table 8

Total Cells in Lung Lavage Fluid[a]
(Values are Mean ± SE)

Aerosol Concentration of Cu-Zn Alloy	N	End of Exposure	After Recovery
0 (Sham)	12	1.04 ± 0.07	1.04 ± 0.05
0.32 mg/m^3	12	0.94 ± 0.03	0.95 ± 0.07
1.0 mg/m^3	12	0.88 ± 0.09	1.17 ± 0.08
3.2 mg/m^3	23-24[c]	1.35 ± 0.10	1.07 ± 0.08
10.0 mg/m^3	12	3.15 ± 0.38[b]	0.94 ± 0.11

[a]Mean ± SE of the total cells in the lavage fluid cell pellet ($\times 10^{-6}$).

[b]The treated groups were compared with the sham-exposed group using Student's t-test for unequal variances when Levene's test indicated the variances were not the same. When Levene's test did not show differences between the variances, Student's t-test for equal variances was used. Probability values were adjusted for multiple comparisons using Bonferroni's inequality; $p < 0.01$.

[c]Twenty-four rats evaluated at the end of exposure, 23 rats after the recovery period.

Table 9

Neutrophil, Lymphocyte, and Macrophage Differentials in Lung Lavage Fluid[a]
(Values are Mean ± SE)

Aerosol Concentration of Cu-Zn Alloy		N	Neutrophils		Lymphocytes		Macrophages	
			End of Exposure	After Recovery	End of Exposure	After Recovery	End of Exposure	After Recovery
0 (Sham)	(percent)	12	0.4 ± 0.1	1.0 ± 0.3	9.5 ± 1.8	6.9 ± 0.9	90.1 ± 1.9	92.1 ± 1.0
	(total)	12	0.004 ± 0.001	0.012 ± 0.004	0.11 ± 0.03	0.07 ± 0.01	0.93 ± 0.05	0.96 ± 0.04
0.32 mg/m^3	(percent)	12	0.4 ± 0.1	0.6 ± 0.2	7.1 ± 1.2	7.8 ± 1.4	92.4 ± 1.1	91.6 ± 1.3
	(total)	12	0.004 ± 0.001	0.006 ± 0.002	0.07 ± 0.01	0.07 ± 0.01	0.87 ± 0.02	0.87 ± 0.07
1.0 mg/m^3	(percent)	12	3.5 ± 0.9[b]	0.8 ± 0.2	5.7 ± 1.0	7.6 ± 1.2	90.3 ± 1.5	91.6 ± 1.2
	(total)	12	0.032 ± 0.010	0.009 ± 0.003	0.05 ± 0.01	0.09 ± 0.01	0.80 ± 0.08	1.07 ± 0.08
3.2 mg/m^3	(percent)	24	3.3 ± 0.5[c]	0.5 ± 0.1	9.9 ± 0.8	10.1 ± 0.8	86.5 ± 0.7	89.4 ± 0.9
	(total)	24	0.043 ± 0.007[c]	0.005 ± 0.001	0.13 ± 0.02	0.11 ± 0.02	1.17 ± 0.09	0.96 ± 0.07
10.0 mg/m^3	(percent)	12	8.8 ± 1.2[c]	0.8 ± 0.3	9.6 ± 1.0	12.7 ± 1.4[c]	81.0 ± 1.4[c]	86.2 ± 1.5[b]
	(total)	12	0.273 ± 0.044[c]	0.007 ± 0.002	0.30 ± 0.04[b]	0.11 ± 0.01	2.56 ± 0.31[c]	0.82 ± 0.11

[a]The above values are differentials taken from the lavage fluid cell pellets (x 10^{-6}).

[b]The treated groups were compared with the sham-exposed group using Student's t-test for unequal variances when Levene's test indicated the variances were not the same. When Levene's test did not show differences between the variances, Student's t-test for equal variances was used. Probability values were adjusted for multiple comparisons using Bonferroni's inequality; $p < 0.05$.

[c]$p < 0.01$.

Table 10

Biochemical Analyses of Bronchoalveolar Lavage Fluid From F344/N Rats That Inhaled Powdered Cu-Zn Alloy

		Aerosol Concentration of Powdered Cu-Zn Alloy, mg/m^3									
		0 (Sham)		0.32		1.0		3.2		10	
Lavage Fluid Constituent	Measure	EOE[a]	REC[a]	EOE	REC	EOE	REC	EOE	REC	EOE	REC
β-Glucuronidase (mIU)	Mean	1.27	1.13	1.62	1.25	1.42	1.86	1.61	1.44	7.08[b]	1.36
	SE	0.15	0.13	0.26	0.16	0.13	0.31	0.16	0.16	1.11	0.28
	N	12	12	12	12	12	12	23	24	12	12
Alkaline Phosphatase (mIU)	Mean	285	269	321	284	411	360	426[b]	254	336	279
	SE	23	21	22	23	42	51	28	15	38	35
	N	12	12	12	12	12	12	23	24	12	12
Lactate Dehydrogenase (mIU)	Mean	385	446	389	488	NU	NU[c]	571	406	NU	NU
	SE	32	21	26	38	NU	NU	63	30	NU	NU
	N	12	12	12	12	NU	NU	12	12	NU	NU
Protein (mg)	Mean	1.54	1.55	1.30	1.51	1.65	1.16	1.70	1.19	2.82[b]	1.21
	SE	0.09	0.15	0.09	0.21	0.09	0.21	0.09	0.09	0.20	0.15
	N	12	12	12	12	12	12	23	24	12	12

[a]EOE means the sampling time was at the end of the 13-week exposure; REC means the sampling time was after the 4-week recovery period.

[b]The treated groups were compared with the sham-exposed group using Student's t-test for unequal variances when Levene's test indicated the variances were not the same. When Levene's test did not show differences between the variances, Student's t-test for equal variances was used. Probability values were adjusted for multiple comparisons using Bonferroni's inequality; $p < 0.01$.

[c]NU = Results not used. No control values were available for Phase III, Part 1 and the values for LDH were considered invalid. Only the values from Phase III, Part 2 are presented for LDH in this table.

Table 11

Collagenous Peptides in Bronchoalveolar Lavage Fluid After 13-Week Exposure to Powdered Cu-Zn Alloy and After 4-Week Recovery Period (Values are Mean ± SE)

Aerosol Concentration of Cu-Zn Alloy	N	Collagenous Peptides in Lavage Fluid: End of Exposure, µg/g Control Lung	End of Exposure, µg/kg Body Weight	After Recovery, µg/g Control Lung	After Recovery, µg/kg Body Weight
0 (Sham)	12	45.4 ± 2.8	216 ± 18	47.6 ± 4.2	199 ± 25
0.32 mg/m^3	12	48.6 ± 2.3	229 ± 15	61.4 ± 9.7	249 ± 33
1.0 mg/m^3	12	63.5 ± 6.0	313 ± 34	68.0 ± 6.8[a]	306 ± 32[a]
3.2 mg/m^3	23	57.5 ± 3.1	276 ± 18	54.5 ± 2.9	235 ± 15
10.0 mg/m^3	12	84.4 ± 6.2[b]	437 ± 38[b]	57.4 ± 3.0	265 ± 20

[a]The treated groups were compared with the sham-exposed group using Student's t-test for unequal variances when Levene's test indicated the variances were not the same. When Levene's test did not show differences between the variances, Student's t-test for equal variances was used. Probability values were adjusted for multiple comparisons using Bonferroni's inequality; $p < 0.05$.

[b]$p < 0.01$.

Table 12 shows the effect of 13 weeks of exposure, followed by a 4-week recovery period, on total lung collagen. No statistically significant changes in total lung collagen were detected for the two exposure levels measured, which were 3.2 and 10 mg Cu-Zn/m^3, the two highest level exposures in Phase III.

4. Immunology and Phagocytosis

The exposure of rats to 10 mg Cu-Zn/m^3 significantly increased the total number of cells present in the lavage fluid (Table 8). However, the increased number of cells in lavage fluid of rats exposed to 10 mg Cu-Zn/m^3 was temporary and returned to normal during the 4-week recovery period.

The increase in the number of cells in lung lavage fluid from rats exposed to 10 mg Cu-Zn/m^3 was due in part to an elevated number of polymorphonuclear leukocytes (neutrophils). Exposures to 0.32 or 1.0 mg Cu-Zn/m^3 did not produce increased numbers of neutrophils in lung lavage fluids, but exposures to 3.2 and 10 mg Cu-Zn/m^3 (Table 9) did increase neutrophil levels. The percentages of neutrophils were normal in all exposed rats after the 4-week recovery period.

The total number of lymphocytes was elevated only in rats exposed to 10 mg Cu-Zn/m^3 (Table 9). This change in numbers of lung lymphocytes present in lavage fluid returned to normal during the 4-week recovery period.

A reduction in the percent and numbers of macrophages in lung lavage fluids was also observed after exposure to 10 mg Cu-Zn/m^3 (Table 9). Even though the percentage of macrophages was reduced, the total number was elevated. The percent of macrophages in lung lavage fluid was still low at the end of the 4-week recovery period, but the number had returned to normal.

Table 12

Total Lung Collagen After 13-Week Exposure to Powdered Cu-Zn Alloy and After 4-Week Recovery Period (Values are Mean ± SE)

Aerosol Concentration of Cu-Zn Alloy	N	Total Lung Collagen[a]			
		End of Exposure		After Recovery	
		mg/g Control Lung	mg/kg Body Weight	mg/g Control Lung	mg/kg Body Weight
0 (Sham)	12[b]	17.4 ± 0.8	76.9 ± 5.7		
0 (Sham)	6	17.2 ± 1.2	81.5 ± 7.6	17.6 ± 1.3	72.3 ± 8.7
3.2 mg/m^3	20	18.7 ± 0.6	89.1 ± 2.9		
10 mg/m^3	10	18.9 ± 0.8	97.3 ± 5.5	17.5 ± 1.1	79.8 ± 6.2

[a]All samples analyzed as a batch after collection of samples for Phase III, Parts 1 and 2.

[b]Results combined for shams evaluated at the end of exposure and shams evaluated after the 4-week recovery period.

Note: The treated groups were compared with the sham-exposed group using the Student's t-test for unequal variances when Levene's test indicated the variances were not the same. When Levene's test did show differences between the variances, Student's t-test for equal variances was used. Probability values were adjusted for multiple comparisons using Bonferroni's inequality.

Total lymphoid cells in lung-associated lymph nodes were increased with exposures to 3.2 and 10 mg Cu-Zn/m^3 (Table 13). This increase was resolved during the recovery period. The only other significant change reflected in the immunology data at the end of exposure was a significant increase in total antibody-forming cells in rats exposed to 10 mg Cu-Zn/m^3, which also returned to normal during the recovery period. The reasons for the observed decrease in antibody-forming cells per million lymphocytes and in total antibody-forming cells after the recovery period for rats exposed to 3.2 and 10 mg Cu-Zn/m^3 are not clear and may have no biological importance relative to inhalation of powdered Cu-Zn alloy.

The results of evaluations of the phagocytic function of macrophages obtained by lung lavage indicated that exposure to 10 mg Cu-Zn/m^3 reduced phagocytic capacity (Table 14). Rats exposed to 0.32 or 1.0 mg Cu-Zn/m^3 had slight, but significantly increased, phagocytic indices at the end of exposure. The reason for this is not known, but probably was associated with a normal response of the respiratory tract defences and had no adverse effects on the rats. There were no significant differences in phagocytosis by alveolar macrophages from any of the groups after the recovery period.

5. Hematology and Serum Chemistry

No significant differences relative to the appropriate comparison (comparisons between groups at the end of exposure, and between groups after four weeks recovery) were noted in the following hematology parameters:

a. Erythrocytes (RBC)

b. Hematocrit (PCV)

c. Hemoglobin

Table 13

Immunology Results for Tracheobronchial Lymph Nodes from Rats in Phase III
(Values are Mean ± SE)

Aerosol Concentration of Cu-Zn Alloy	N	Total Lymphoid Cells x 10^{-6}		Antibody-Forming Cells Per Million Lymphocytes		Total Antibody-Forming Cells	
		EOE[a]	REC[a]	EOE	REC	EOE	REC
0 (Sham)	8	8.78 ± 0.71	10.00 ± 0.71	517 ± 104	1110 ± 237	4840 ± 1170	11200 ± 2740
1.0 mg/m^3	6-7[b]	8.21 ± 1.11	9.40 ± 1.72	1080 ± 327	907 ± 313	9360 ± 3490	10250 ± 5020
3.2 mg/m^3	15	15.58 ± 1.39[c]	8.06 ± 0.73	598 ± 103	447 ± 94[d]	9810 ± 2020	4210 ± 1100
10.0 mg/m^3	7-8[e]	27.09 ± 3.43[c]	10.09 ± 0.51	884 ± 115	369 ± 115[d]	23300 ± 3540[c]	3930 ± 1290

[a]EOE means the sampling time was at the end of the 13-week exposure; REC means the sampling time was after the 4-week recovery period.

[b]N = 7 at end of exposure; N = 8 for recovery.

[c]The treated groups were compared with the sham-exposed group using Student's t-test for unequal variances when Levene's test indicated the variances were not the same. When Levene's test did not show differences between the variances, Student's t-test for equal variances was used. Probability values were adjusted for multiple comparisons using Bonferroni's inequality; $p < 0.01$.

[d]$p < 0.05$.

[e]N = 7 at end of exposure; N = 6 for recovery.

Table 14

Macrophage Phagocytosis of Opsonized Sheep Red Blood Cells[a]
(Values are Mean ± SE)

Aerosol Concentration of Cu-Zn Alloy	N	Numbers		Percentages	
		End of Exposure	After Recovery	End of Exposure	After Recovery
0 (Sham)	12	367 ± 20	404 ± 27	74.4 ± 1.9	81.8 ± 2.5
0.32 mg/m^3	12	490 ± 25[b]	395 ± 32	79.9 ± 1.2	82.0 ± 2.2
1.0 mg/m^3	12	481 ± 30[b]	341 ± 30	80.5 ± 1.5	76.0 ± 2.1
3.2 mg/m^3	24	405 ± 21	362 ± 28	72.4 ± 1.9	80.1 ± 2.2
10.0 mg/m^3	12	251 ± 16[b]	299 ± 16	60.2 ± 3.6[c]	73.2 ± 1.9

[a]The above values show the numbers of opsonized sheep red blood cells phagocytized by 100 macrophages and the percentages of macrophages that phagocytized the cells.

[b]The treated groups were compared with the sham-exposed group using Student's t-test for unequal variances when Levene's test indicated the variances were not the same. When Levene's test did not show differences between the variances, Student's t-test for equal variances was used. Probability values were adjusted for multiple comparisons using Bonferroni's inequality; $p < 0.05$.

[c]$p < 0.01$.

d. Mean corpuscular volume

e. Leukocyte (WBC) count

f. Differential cells of the blood smear (neutrophils, eosinophils, lymphocytes, monocytes, and nucleated erythrocytes [NRBC])

Also, there were no significant dose-related responses in any of the parameters analyzed for serum chemistry. These parameters were:

a. Alkaline phosphatase

b. Serum glutamic pyruvic transaminase

c. Total bilirubin

d. Blood urea nitrogen

e. Protein and albumin

Data for individual rats for the hematology and serum chemistry results are included in Appendix E. Since there were no differences to discuss, tabulated results for these parameters were not included in the text of the report.

6. Respiratory Function Measurements

Tables 15 through 18 summarize selected results of respiratory function evaluations. Detailed results for all of the measurements are included in the Appendix. Few statistically significant differences ($p \leq 0.05$) or consistent trends related to the exposures were observed. Therefore, parameters representing key indices of respiratory function were selected for display in Tables 15 through 18. These parameters included lung volume (total lung capacity, vital capacity and functional residual capacity), lung stiffness (dynamic and quasistatic compliance), alveolar-capillary gas

Table 15

Respiratory Function Results for F344/N Rats in Phase III, Parts 1 and 2 Combined (Baseline Measurements) (Mean ± SE)

		Aerosol Concentration of Powdered Cu-Zn Alloy, mg/m^3			
Parameter	Units	0 (Sham) (N = 32)[a]	1.0 (N = 16)	3.2 (N = 32)	10 (N = 16)
Total Lung Capacity (TLC)	mL	10.4 ± 0.3	11.1 ± 0.3	10.8 ± 0.3	11.1 ± 0.3
Vital Capacity/TLC	percent	88.7 ± 0.9	87.7 ± 0.8	87.0 ± 1.1	87.4 ± 0.7
Functional Residual Capacity	mL	2.2 ± 0.1	2.3 ± 0.1	2.4 ± 0.1	2.4 ± 0.1
Dynamic Lung Compliance	mL/cm H_2O	0.43 ± 0.03	0.42 ± 0.03	0.46 ± 0.04	0.41 ± 0.03
Quasistatic Chord Compliance	mL/cm H_2O	0.59 ± 0.02	0.64 ± 0.02	0.61 ± 0.02	0.63 ± 0.02
CO Diffusing Capacity (DLCO)	mL/min/mm Hg	0.18 ± 0.01	0.19 ± 0.01	0.18 ± 0.01	0.19 ± 0.01
DLCO/Lung Volume	DLCO/mL	0.018 ± 0.001	0.017 ± 0.001	0.017 ± 0.001	0.017 ± 0.001
DLCO/kg Body Weight	DLCO/kg	0.80 ± 0.02	0.85 ± 0.03	0.80 ± 0.02	0.83 ± 0.02
Forced Vital Capacity Exhaled in 0.1 Second	percent	73.8 ± 1.1	72.8 ± 2.0	70.9 ± 1.9	71.9 ± 2.8
Mean Midexpiratory Flow (MMEF)	mL/sec	67.2 ± 2.2	72.6 ± 4.1	67.4 ± 3.5	70.9 ± 5.3
MMEF/Forced Vital Capacity	mL/sec/mL	7.3 ± 0.2	7.3 ± 0.4	7.0 ± 0.3	7.1 ± 0.6
Slope of Phase III of Single-Breath N_2 Washout	percent/N_2/mL	85.8 ± 8.5	97.3 ± 5.5	80.7 ± 4.9	98.7 ± 6.1

[a]Shams from Phase III, Parts 1 and 2 were all used for comparisons of baseline measurements.

Note: The treated groups were compared with the sham-exposed group using Student's t-test for unequal variances when Levene's test indicated the variances were not the same. When Levene's test did not show differences between the variances, Student's t-test for equal variances was used. Probability values were adjusted for multiple comparisons using Bonferroni's inequality.

Table 16

Respiratory Function Results for F344/N Rats in Phase III, Parts 1 and 2 Combined (Week Seven of Exposures) (Mean ± SE)

Parameter	Units	Aerosol Concentration of Powdered Cu-Zn Alloy, mg/m^3 0 (Sham) (N = 32)[a]	1.0 (N = 16)	3.2 (N = 32)	10 (N = 16)
Total Lung Capacity (TLC)	mL	12.1 ± 0.5	11.4 ± 0.4	12.5 ± 0.4	11.1 ± 0.3
Vital Capacity/TLC	percent	92.8 ± 0.4	91.6 ± 0.7	92.2 ± 0.5	90.9 ± 0.7
Functional Residual Capacity	mL	2.4 ± 0.1	2.2 ± 0.1	2.4 ± 0.1	2.3 ± 0.1
Dynamic Lung Compliance	mL/cm H_2O	0.46 ± 0.03	0.41 ± 0.03	0.48 ± 0.03	0.39 ± 0.02
Quasistatic Chord Compliance	mL/cm H_2O	0.72 ± 0.03	0.66 ± 0.03	0.74 ± 0.03	0.64 ± 0.02
CO Diffusing Capacity (DLCO)	mL/min/mm Hg	0.21 ± 0.01	0.21 ± 0.01	0.21 ± 0.01	0.19 ± 0.01
DLCO/Lung Volume	DLCO/mL	0.018 ± 0.001	0.018 ± 0.001	0.017 ± 0.001	0.017 ± 0.001
DLCO/kg Body Weight	DLCO/kg	0.89 ± 0.02	0.92 ± 0.02	0.91 ± 0.02	0.83 ± 0.02
Forced Vital Capacity Exhaled in 0.1 Second	percent	71.1 ± 1.0	69.4 ± 2.3	68.8 ± 1.4	72.7 ± 1.5
Mean Midexpiratory Flow (MMEF)	mL/sec	78.6 ± 2.9	76.4 ± 4.5	77.5 ± 3.2	78.1 ± 2.3
MMEF/Forced Vital Capacity	mL/sec/mL	6.9 ± 0.2	6.8 ± 0.4	6.7 ± 0.3	7.4 ± 0.3
Slope of Phase III of Single-Breath N_2 Washout	percent/N_2/mL	71.8 ± 3.3	82.6 ± 5.8	71.7 ± 3.3	81.4 ± 4.8

[a]Shams from Phase III, Parts 1 and 2 were all used for comparisons of baseline measurements.

Note: The treated groups were compared with the sham-exposed group using Student's t-test for unequal variances when Levene's test indicated the variances were not the same. When Levene's test did not show differences between the variances, Student's t-test for equal variances was used. Probability values were adjusted for multiple comparisons using Bonferroni's inequality.

Table 17

Respiratory Function Results for F344/N Rats in Phase III, Parts 1 and 2 Combined (End of Exposure) (Mean ± SE)

Parameter	Units	Aerosol Concentration of Powdered Cu-Zn Alloy, mg/m^3: 0 (Sham) (N = 16)	1.0 (N = 16)	3.2 (N = 32)	10 (N = 16)
Total Lung Capacity (TLC)	mL	11.4 ± 0.5	11.7 ± 0.4	11.7 ± 0.3	11.2 ± 0.4
Vital Capacity/TLC	percent	91.8 ± 1.1	93.2 ± 0.9	93.6 ± 0.6	92.1 ± 0.7
Functional Residual Capacity	mL	2.2 ± 0.1	2.1 ± 0.1	2.1 ± 0.1	2.1 ± 0.1
Dynamic Lung Compliance	mL/cm H_2O	0.41 ± 0.03	0.40 ± 0.02	0.43 ± 0.02	0.37 ± 0.03
Quasistatic Chord Compliance	mL/cm H_2O	0.68 ± 0.02	0.71 ± 0.03	0.72 ± 0.02	0.68 ± 0.03
CO Diffusing Capacity (DLCO)	mL/min/mm Hg	0.25 ± 0.01	0.22 ± 0.01	0.25 ± 0.01	0.20 ± 0.01
DLCO/Lung Volume	DLCO/mL	0.022 ± 0.001	0.019 ± 0.001	0.021 ± 0.001	0.017 ± 0.001[a]
DLCO/kg Body Weight	DLCO/kg	0.96 ± 0.03	0.92 ± 0.04	0.96 ± 0.02	0.81 ± 0.03[a]
Forced Vital Capacity Exhaled in 0.1 Second	percent	73.1 ± 1.8	67.5 ± 2.2	67.1 ± 1.4	64.8 ± 2.5
Mean Midexpiratory Flow (MMEF)	mL/sec	73.7 ± 2.0	73.8 ± 5.2	68.4 ± 3.0	63.6 ± 5.0
MMEF/Forced Vital Capacity	mL/sec/mL	7.4 ± 0.4	6.4 ± 0.4	6.2 ± 0.3	5.9 ± 0.5
Slope of Phase III of Single-Breath N_2 Washout	percent/N_2/mL	70.0 ± 5.4	67.4 ± 5.9	69.5 ± 4.9	69.4 ± 6.6

Note: The treated groups were compared with the sham-exposed group using Student's t-test for unequal variances when Levene's test indicated the variances were not the same. When Levene's test did not show differences between the variances, Student's t-test for equal variances was used. Probability values were adjusted for multiple comparisons using Bonferroni's inequality.

[a]$p < 0.01$.

Table 18

Respiratory Function Results for F344/N Rats in Phase III, Parts 1 and 2 Combined (After Recovery) (Mean ± SE)

Parameter	Units	Aerosol Concentration of Powdered Cu-Zn Alloy, mg/m^3: 0 (Sham) (N = 16)	1.0 (N = 16)	3.2 (N = 32)	10 (N = 16)
Total Lung Capacity (TLC)	mL	11.2 ± 0.4	12.5 ± 0.5	12.4 ± 0.4	12.7 ± 0.5
Vital Capacity/TLC	percent	92.8 ± 0.7	88.7 ± 0.9[a]	90.5 ± 0.6	88.6 ± 0.6[a]
Functional Residual Capacity	mL	2.1 ± 0.1	2.7 ± 0.1[b]	2.5 ± 0.1[a]	2.7 ± 0.1[b]
Dynamic Lung Compliance	mL/cm H_2O	0.39 ± 0.03	0.43 ± 0.04	0.44 ± 0.03	0.40 ± 0.04
Quasistatic Chord Compliance	mL/cm H_2O	0.68 ± 0.02	0.75 ± 0.03	0.74 ± 0.02	0.78 ± 0.03
CO Diffusing Capacity (DLCO)	mL/min/mm Hg	0.24 ± 0.01	0.23 ± 0.02	0.22 ± 0.01	0.22 ± 0.01
DLCO/Lung Volume	DLCO/mL	0.022 ± 0.001	0.018 ± 0.001	0.018 ± 0.001	0.017 ± 0.001[a]
DLCO/kg Body Weight	DLCO/kg	0.88 ± 0.03	0.88 ± 0.06	0.83 ± 0.04	0.84 ± 0.05
Forced Vital Capacity Exhaled in 0.1 Second	percent	67.8 ± 2.5	67.9 ± 1.7	65.4 ± 1.8	70.8 ± 1.8
Mean Midexpiratory Flow (MMEF)	mL/sec	65.8 ± 4.6	77.7 ± 2.7	71.0 ± 4.2	84.7 ± 2.5[a]
MMEF/Forced Vital Capacity	mL/sec/mL	6.5 ± 0.5	6.4 ± 0.3	6.0 ± 0.3	7.0 ± 0.3
Slope of Phase III of Single-Breath N_2 Washout	percent/N_2/mL	65.0 ± 4.5	63.2 ± 5.4	63.7 ± 3.8	57.0 ± 4.4

Note: The treated groups were compared with the sham-exposed group using Student's t-test for unequal variances when Levene's test indicated the variances were not the same. When Levene's test did not show differences between the variances, Student's" -test for equal variances was used. Probability values were adjusted for multiple comparisons using Bonferroni's inequality.

[a] $p < 0.05$.

[b] $p < 0.01$.

exchange (CO diffusing capacity), airflow restriction (percentage of forced vital capacity exhaled in 0.1 second and mean midexpiratory flow), and intrapulmonary gas distribution (slope of single-breath nitrogen washout). Detailed results for all of the measurements are included in the Appendix.

There were no statistically significant differences among the mean values of respiratory function parameters of the four groups before exposures began (Table 15) or after seven weeks of exposure (Table 16).

After 13 weeks of exposure (Table 17), the only significant differences between control and exposed groups were increased DLCO/lung volume and DLCO/body weight ratios in the rats exposed to 10 mg Cu-Zn/m^3. The CO diffusing capacity, lung weight, and body weight of the 10 mg/m^3 group were slightly, but nonsignificantly lower than that of the other groups; therefore the significant difference was a statistical result of the combination of nonsignificant differences in lung and body weights and CO diffusing capacity. Since CO diffusing capacity is affected by lung volume, the most useful size-normalized parameter is the diffusing capacity divided by lung volume (DLCO/lung volume). This parameter was significantly reduced in the group exposed to 10 mg Cu-Zn/m^3 at the end of exposure (Table 17) and after the recovery period (Table 18).

7. Necropsy and Histopathology

Table 19 presents results for body and organ weights at the time of sacrifice for rats used for histopathologic evaluations in Phase III, Parts 1 and 2. Results for individual animals are detailed in the Appendix. Comparisons among these subsets of rats from the 3 exposure groups in Part 1 indicated no significant differences in body weights at the end of exposure or after the recovery period. The same result was seen for the 3 subsets of rats

Table 19

Body and Organ Weight Summary for Phase III, Parts 1 and 2 for End of Exposure (EOE) and After Recovery (REC)[a]
(Values are Mean ± SE)

Animal Sex	Body and Organ Weights (g)	SAC Code[b]	Aerosol Concentration of Powdered Cu-Zn Alloy, mg/m^3 — Phase III, Part 1: 1.0	Phase III, Part 1: 3.2	Phase III, Part 1: 10	Phase III, Part 2: 0 (Sham)	Phase III, Part 2: 0.32	Phase III, Part 2: 3.2
Female	Body Weight	EOE	189 ± 4.9	188 ± 2.0[c]	183 ± 2.1	195 ± 1.4	195 ± 2.3	194 ± 1.6
		REC	192 ± 1.9	198 ± 3.2	190 ± 2.4	206 ± 2.0	205 ± 2.5	203 ± 1.4
	Lung	EOE	0.97 ± 0.03	1.06 ± 0.03	1.14 ± 0.02[d]	1.05 ± 0.03	0.99 ± 0.04	1.05 ± 0.02
		REC	0.94 ± 0.03	0.96 ± 0.02	1.00 ± 0.03	1.07 ± 0.03	1.05 ± 0.04	1.11 ± 0.04
	Brain	EOE	1.75 ± 0.02	1.76 ± 0.01	1.74 ± 0.01	1.79 ± 0.03	1.74 ± 0.01	1.75 ± 0.01
		REC	1.77 ± 0.01	1.76 ± 0.01	1.74 ± 0.03	1.80 ± 0.01	1.81 0.01	1.83 ± 0.01
	Kidneys	EOE	1.39 ± 0.03	1.39 ± 0.01	1.39 ± 0.02	1.39 ± 0.02	1.40 ± 0.03	1.39 ± 0.02
		REC	1.43 ± 0.03	1.46 ± 0.04	1.39 ± 0.02	1.45 ± 0.08	1.43 ± 0.08	1.51 ± 0.02
	Liver	EOE	5.37 ± 0.08	5.51 ± 0.08	5.49 ± 0.07	5.77 ± 0.09	5.80 ± 0.14	5.72 ± 0.12
		REC	5.49 ± 0.11	5.72 ± 0.13	5.39 ± 0.15	6.30 ± 0.17	6.40 ± 0.10	6.31 ± 0.10
	Ovaries	EOE	0.06 ± 0.006	0.05 ± 0.003	0.06 ± 0.004	0.05 ± 0.004	0.05 ± 0.004	0.06 ± 0.003
		REC	0.005 ± 0.003	0.06 ± 0.004	0.05 ± 0.003	0.06 ± 0.003	0.06 ± 0.004	0.06 ± 0.004
Male	Body Weight	EOE	312 ± 4.5	313 ± 3.9	296 ± 2.8	331 ± 2.4	334 ± 3.2	329 ± 2.5[c]
		REC	325 ± 5.5	335 ± 4.0[c]	329 ± 3.8	367 ± 5.4	358 ± 5.2	361 ± 3.7
	Lung	EOE	1.34 ± 0.07	1.36 ± 0.03	1.55 ± 0.04[e]	1.42 ± 0.03	1.46 ± 0.04[c]	1.47 ± 0.07
		REC	1.28 ± 0.04	1.31 ± 0.02	1.45 ± 0.03	1.50 ± 0.04	1.51 ± 0.07[c]	1.52 ± 0.04
	Brain	EOE	1.93 ± 0.01	1.90 ± 0.02	1.88 ± 0.02	1.93 ± 0.01	1.90 ± 0.01	1.91 ± 0.01
		REC	1.86 ± 0.07	1.89 ± 0.01	1.91 ± 0.01	2.00 ± 0.01	1.95 ± 0.01	1.97 ± 0.02
	Kidneys	EOE	2.11 ± 0.05	2.12 ± 0.04	2.05 ± 0.03	2.21 ± 0.04	2.15 ± 0.03	2.19 ± 0.04
		REC	2.13 ± 0.05	2.22 ± 0.05	2.24 ± 0.06	2.49 ± 0.06	2.21 ± 0.12	2.28 ± 0.12
	Liver	EOE	9.86 ± 0.23	9.71 ± 0.19	9.53 ± 0.15	10.24 ± 0.28	10.39 ± 0.10	10.15 ± 0.24
		REC	9.73 ± 0.27	10.40 ± 0.25	10.08 ± 0.26	12.04 ± 0.22	11.51 ± 0.34	11.66 ± 0.19
	Testes	EOE	1.39 ± 0.05	1.38 ± 0.04	1.39 ± 0.02	1.41 ± 0.04	1.48 ± 0.01	1.53 ± 0.03
		REC	1.38 ± 0.04	1.39 ± 0.05	1.41 ± 0.02	1.53 ± 0.04	1.71 ± 0.09[c]	1.67 ± 0.09

[a]Exposures were for 13 weeks, the recovery period was 4 weeks after the last nose-only inhalation exposure. Exposures were to aerosols containing 0 (sham), 0.32, 1.0, 3.2, or 10 mg Cu-Zn alloy powder/m^3.

[b]EOE means the sampling time was at the end of the 13-week exposure; REC means the sampling time was after the 4-week recovery period.

[c]N = 10; N = 11 for all other groups.

[d]The treated groups were compared with the lowest-level exposure group (Part 1) or with the sham-exposed group (Part 2) using Student's t-test for unequal variances when Levene's test indicated the variances were not the same. When Levene's test did not show differences between the variances, Student's t-test for equal variances was used. Probability values were adjusted for multiple comparisons using Bonferroni's inequality; $p < 0.01$.

[e]$p \leq 0.05$.

from Phase III, Part 2. The rats exposed to 10 mg Cu-Zn/m^3 had body weights that appeared low relative to the other two groups in Phase III, Part 1. However, these apparent decreased body weights (for both males and females) were not statistically different from the other two groups.

Body weight comparisons using body weights for all of the rats in Phase III, Part 1 indicated exposure to 10 mg Cu-Zn/m^3 caused a decreased body weight by the end of the 13-week exposure (Table 7). Rats in all exposure groups showed increased body weight during the 4-week recovery period and were not significantly different from each other after the recovery period.

Organ weights, with the exception of lung, showed no exposure-related changes. The organ weights were slightly elevated after the 4-week recovery period, reflecting the increases in animal body weight during the recovery period. As compared with rats exposed to 1.0 mg Cu-Zn/m^3, the lung weights of rats exposed to 10 mg Cu-Zn/m^3 were significantly increased at the end of the 13-week exposure period ($p \leq 0.05$ for males and $p \leq 0.01$ for females). In both sexes, the lung weights were not significantly different from the other two exposure groups in Phase III, Part 1 at the end of the 4-week recovery period. There were no significant differences at the end of exposure or after the recovery period in lung weights of rats sham-exposed, or exposed to Cu-Zn in Phase III, Part 2.

Lesions produced by Cu-Zn inhaled by rats were produced only in nasal epithelium and lungs (Table 20). A summary of the fractions of rats in each exposure group with induced lesions, the average severity of those specific lesions, and the overall average severity scores for the lesions are presented in Table 20. The principal microscopic lesions were atrophy of the olfactory epithelium in a focal region of the nasal cavity, alveolar

Table 20

Summary of Respiratory Tract Lesions in F344/N Rats After 13-Weeks Exposure to Aerosols of Powdered Cu-Zn Alloy and After a 4-Week Recovery Period

Lesion	Measure	Aerosol Concentration of Cu-Zn Alloy Powder, mg/m^3				
		0 (Sham)	0.32	1.0	3.2	10
End of Exposure						
Nasal Epithelium Atrophy	Frequency of Lesions[a]	0/22	0/22	3/22	6/44	15/22
	Average Severity[b]			1.0	1.0	1.2
	Overall Severity[c]			0.14 ± 0.08	0.14 ± 0.05	0.82 ± 0.14[d]
Alveolar Macrophage Hyperplasia	Frequency of Lesions	1/22	0/22	0/22	24/44	18/22
	Average Severity	1.0			1.0	1.4
	Overall Severity	0.05 ± 0.05			0.55 ± 0.08[d]	1.14 ± 0.15[d]
Type II Pneumocyte Hyperplasia	Frequency of Lesions	0/22	0/22	0/22	12/44	17/22
	Average Severity				1.0	1.2
	Overall Severity				0.27 ± 0.07[d]	0.91 ± 0.13[d]
Alveolitis	Frequency of Lesions	0/22	0/22	0/22	11/44	18/22
	Average Severity				1.0	1.4
	Overall Severity				0.25 ± 0.07	1.14 ± 0.15
After Recovery						
Nasal Epithelium Atrophy	Frequency of Lesions	0/22	0/22	0/22	1/43	7/22
	Average Severity				1.0	1.1
					0.02 ± 0.02	0.36 ± 0.12
Alveolar Macrophage Hyperplasia	Frequency of Lesions	3/22	1/22	0/22	10/43	22/22
	Average Severity	1.0	1.0		1.0	1.0
	Overall Severity	0.14 ± 0.08	0.05 ± 0.05		0.23 ± 0.07	1.05 ± 0.05[d]
Type II Pneumocyte Hyperplasia	Frequency of Lesions	0/22	1/22	1/22	8/43	22/22
	Average Severity		1.0	1.0	1.0	1.0
	Overall Severity		0.05 ± 0.05	0.05 ± 0.05	0.19 ± 0.06[e]	1.05 ± 0.05[d]
Alveolitis	Frequency of Lesions	0/22	1/22	0/22	1/43	0/22
	Average Severity		1.0		1.0	
	Overall Severity		0.05 ± 0.05		0.02 ± 0.02	

[a]Fraction of rats in each group that developed the lesion.

[b]Average severity score for rats with lesions having a rating of 1 or more. The lesion rating was: 0 = no change relative to normal, lesion not present; 1 = slight degree of change, or small amount present; 2 = moderate, median, or middle severity or amount; 3 = marked severity or degree of change, large amount present.

[c]Overall severity represents the mean ± SE for the severity rating for each rat, including those rats with severity ratings of zero.

[d]The treated groups were compared with the sham-exposed group using Student's t-test for unequal variances if Levene's test indicated the variances were not the same. When Levene's test did not show differences between the variances, Student's t-test for equal variances was used. Probability values were adjusted for multiple comparisons using Bonferroni's inequality; $p < 0.01$.

[e]$p < 0.05$.

macrophage hyperplasia, type II pneumocyte hyperplasia, and a focal necrotizing alveolitis. Fifteen of 22 rats exposed to 10 mg Cu-Zn/m^3, 6 of 44 rats exposed to 3.2 mg Cu-Zn/m^3, and 3 of 22 rats exposed to 1.0 mg Cu-Zn/m^3 had nasal epithelial atropy at the end of exposure. Although the number of rats with this lesion was greater in the group exposed to 10 mg Cu-Zn/m^3, as compared with rats exposed to 3.2 or 1.0 mg/m^3, there were no significant differences in the severity of the lesion. After the recovery period, this lesion was present in 7 of 22 rats exposed to 10 mg Cu-Zn/m^3 and 1 of 43 rats exposed to 3.2 mg Cu-Zn/m^3. At the end of the exposure period, alveolar macrophage hyperplasia was found in 18 of 22 rats exposed to 10 mg Cu-Zn/m^3 and 24 of 44 rats exposed to 3.2 mg Cu-Zn/m^3. This lesion did not resolve during the 4-week recovery period in rats exposed to 10 mg Cu-Zn/m^3, but appeared to partially resolve in rats exposed to 3.2 mg Cu-Zn/m^3. Type II pneumocyte hyperplasia was observed at the end of the exposure in 17 of 22 rats exposed to 10 mg Cu-Zn/m^3 and 12 of 44 rats exposed to 3.2 mg Cu-Zn/m^3. This lesion also persisted during the recovery period. Alveolitis was present at the end of exposure in 18 of 22 rats exposed to 10 mg Cu-Zn/m^3 and in 11 of 44 rats exposed to 3.2 mg Cu-Zn/m^3. This lesion resolved during the recovery period. Type II pneumocyte hyperplasia, macrophage hyperplasia, and alveolitis were not present in rats after exposure to 1.0 or 0.32 mg Cu-Zn/m^3 for 13 weeks. However, the lesions were observed in a small number of rats after the recovery period. The numbers were not statistically significant and the lesion severity score was "slight degree of change". The reason these lesions were observed after the recovery period is not known, but we conclude that they were not progressively developing or delayed lesions produced by exposures to Cu-Zn since (1) they were not present in rats evaluated at the

end of the exposure period, and (2) the lesions were seen in sham-exposed rats to the same extent as they were seen in rats exposed to Cu-Zn alloy.

No exposure-induced lesions or alterations were evident in the tissue sections of larynx, trachea, or tracheobronchial lymph nodes of any of the experimental groups.

8. Lung Burdens of Cu and Zn

Results for lung content of Cu and Zn for rats analyzed at the end of the 13-week exposure series and 4 weeks later are presented in Table 21. The amounts of Cu and Zn in rats exposed to 1.0, 3.2 and 10 mg Cu-Zn/m^3 were not significantly different from controls and were not significantly different from each other at the end of exposure or after the 4-week recovery period.

Table 21

Lung Content of Cu and Zn in F344/N Rats Exposed
Nose-Only in Phase III, Part 1

Aerosol Concentration of Cu-Zn Alloy	N	Measure	μg At End of Exposure[a]			μg After 4 Weeks Recovery		
			Cu	Zn	Cu+Zn	Cu	Zn	Cu+Zn
0 (Sham)	12	Mean	2.12	23.85	25.96	NS[b]	NS	NS
		SE	0.16	0.84	0.88	--	--	--
1.0 mg/m^3	6-7[c]	Mean	1.74	20.84	22.57	0.99	18.74	19.73
		SE	0.22	2.17	2.28	0.11	0.55	0.62
3.2 mg/m^3	7-8[d]	Mean	2.36	21.14	23.50	1.25	17.52	18.77
		SE	0.36	1.01	1.03	0.18	0.74	0.86
10 mg/m^3	8	Mean	2.31	21.87	24.18	1.23	18.08	19.32
		SE	0.28	1.70	1.79	0.18	0.75	0.84

[a]Samples for shams taken from rats that died during exposure one day before the last scheduled exposure.

[b]No samples for shams after the recovery period, since no animals were available for this evaluation.

[c]N = 7 for end of exposure; N = 6 for after recovery.

[d]N = 7 for end of exposure; N = 8 for after recovery.

Note: The treated groups were compared with the sham-exposed group using Student's t-test for unequal variances if Levene's test indicated the variances were not the same. When Levene's test did show differences between the variances, Student's t-test for equal variances was used. Probability values were adjusted for multiple comparisons using Bonferroni's inequality.

VII. GENERAL DISCUSSION AND CONCLUSIONS

Phase I of this project used exposures of F344/N rats to 100 mg Cu-Zn/m^3, with exposures 2.5 hours/day, for 2 or 5 days (Snipes et al., 1987). The weekly concentration x time (C x T) product in Phase I was 1250 mg·hr Cu-Zn/m^3. Adverse effects were produced in the upper respiratory tracts and pulmonary regions of those rats after 2 days of exposure. Similar responses to inhaled Cu-Zn were noted in Phase II (Snipes et al., 1988), where experimental conditions included aerosol concentrations of 10 or 40 mg Cu-Zn/m^3 and exposures 2 or 4 days/week, 1.5 or 3 hours/day for 4 weeks. The weekly C x T products in Phase II were 0 (sham), 30, 60, 120, 240, and 480 mg·hr Cu-Zn/m^3. The 60, 120, and 240 weekly C x T product exposures were produced using both 2 and 4 exposures/week. This provided the opportunity to compare effects of exposure frequency on biological responses for the same C x T product. Results of Phase II showed that exposures to Cu-Zn alloy 4 days/week were more detrimental to the rats than exposures 2 days/week for the same C x T product. Also, exposures to at least 60 mg·hr Cu-Zn/week were generally needed to produce significant biological responses in F344/N rats exposed for a period of 4 weeks.

Based primarily on the results from Phase II, the subacute exposures of F344/N rats in Phase III were designed to have a maximum weekly exposure of 60 mg·hr Cu-Zn/m^3. The rats were exposed 1.5 hours/day, 4 days/week for 13 weeks to aerosols of Cu-Zn alloy containing 0 (sham), 0.32, 1.0, 3.2, or 10 mg/m^3. The purpose of Phase III was to determine adverse effects of exposures to the defined air concentrations of Cu-Zn alloy by measuring specific biological parameters after the 13 weeks of exposure. In addition to evaluating the rats after the 13-week exposures, additional rats were evaluated 4 weeks later to determine if biological damage would resolve during that time period.

The Cu-Zn alloy did not accumulate in the lungs of rats. The aerosol size distributions were in the range of sizes that would be highly respirable by rats. Even with a small deposition fraction for the inhaled material, the daily lung deposition for rats inhaling 10 mg Cu-Zn/m^3 would have been several μg. During the 13-week exposure, rats would have deposited mg quantities of Cu-Zn in their lungs. The absence of significant amounts of either metal after 13 weeks of exposure to aerosol concentrations as high as 10 mg Cu-Zn/m^3 indicated rapid clearance of the particles of metal powder from the rat lung.

No exposure-related changes were seen in any of the serum chemistry data (alkaline phosphatase, serum glutamic pyruvic transaminase, total bilirubin, blood urea nitrogen, protein, and albumin). Values were all considered to be within the normal range for these blood serum parameters, and we conclude that the exposures to Cu-Zn had no effect on the rats that could be detected by these blood serum chemistry analyses. Bronchoalveolar lavage fluid analyses indicated a transient, exposure related inflammatory response to the inhaled Cu-Zn. The lowest exposure concentration producing significant evidence of the inflammatory response was 3.2 mg Cu-Zn/m^3. The inflammatory response was completely resolved within 4 weeks after the last inhalation exposure to Cu-Zn.

Airway (lavage fluid) collagenous peptides were increased in rats after 13 weeks of exposure to 10 mg Cu-Zn/m^3. Since airway collagenous peptides are soluble hydroxyproline-containing compounds which have leaked into alveoli and small airways, they probably represent turnover of the extracellular collagenous matrix associated with alveolitis and macrophage hyperplasia. Following 4 weeks of recovery, this increase in collagenous peptides had disappeared in rats exposed to 10 mg Cu-Zn/m^3 but was seen in rats exposed to 1.0 mg Cu-Zn/m^3. The reason for this is unknown and it was not thought to represent an adverse effect related to the aerosol exposures.

At the end of the exposures to 10 mg Cu-Zn/m^3, the total numbers of lymphocytes were increased in bronchoalveolar lavage fluid. This has been observed after inhalation of other aerosols, such as diesel exhaust, fly ash, and silica (Bice et al., 1985, 1987). However, the lymphocyte levels returned to normal during the four-week recovery period, indicating that the response was quickly resolved after exposures to Cu-Zn ended. In contrast, exposure to fly ash and silica resulted in permanently increased numbers of lymphocytes in the lung-associated lymph nodes (Bice et al., 1987). Immunology results all indicated that inhalation of Cu-Zn had minimal effects on the lung-associated lymph nodes, showing increased immune responses rather than immune suppression. The elevated immune response at the end of exposure to 10 mg Cu-Zn/m^3 was not permanent and returned to normal during the 4-week recovery period following the 13-week inhalation exposure series.

Macrophage phagocytic ability was significantly increased by exposures to 0.32 or 1.0 mg Cu-Zn/m^3, and was decreased by exposure to 10 mg Cu-Zn/m^3. This response at the lower concentrations was not considered detrimental and may represent a normal response to inhaled materials, where the presence of foreign particles in the lung stimulates phagocytic activity. The exposures to 10 mg Cu-Zn/m^3 depressed phagocytic ability of pulmonary macrophages, which represents an adverse effect. No significant differences existed among the sham-exposed and Cu-Zn-exposed rats after the 4-week recovery period.

Exposure to 10 mg Cu-Zn/m^3 resulted in reduced carbon monoxide diffusing capacity in these rats, which persisted and did not resolve during the 4-week recovery period. The reduced DLCO/lung volume and DLCO/body weight ratios suggested an impairment of alveolar-capillary gas exchange at the membrane level. These findings are consistent with pathology of the lung parenchyma,

but are not specific for a single type of lesion. The magnitudes of the functional changes were small. A human subject with respiratory functional changes of a similar nature and magnitude would not likely present symptoms.

Thirteen weeks of inhalation exposure 1.5 hours/day, 4 days/week to 3.2 or 10 mg Cu-Zn/m^3 produced histologic evidence of olfactory epithelial atrophy, alveolitis, macrophage hyperplasia, and type II pneumocyte hyperplasia in lung parenchyma. The focal alveolitis was associated with terminal bronchioles, proximal alveolar ducts, and adjacent alveoli. Following 4 weeks of recovery, olfactory epithelial atrophy and alveolitis had partially resolved. In contrast, alveolar macrophage hyperplasia and type II pneumocyte hyperplasia did not resolve rapidly, and these lesions were still seen after the recovery period.

The only significant lesion produced in these F344/N rats by inhalation of less than 3.2 mg Cu-Zn/m^3 was nasal epithelial atrophy, produced in 3 of 22 rats exposed to 1.0 mg Cu-Zn/m^3. The lesion fully resolved by the end of the 4-week recovery period. The lesions observed in sham-exposed rats and rats exposed to 0.32 or 1.0 mg Cu-Zn/m^3 did not appear to be related to the inhalation of Cu-Zn and did not appear to have long-term adverse health implications. For example, one of 22 sham-exposed rats had a slight alveolar macrophage hyperplasia at the end of exposure, but none of the rats exposed to 0.32 or 1.0 mg Cu-Zn/m^3 had the lesion at that time. After the 4-week recovery period, alveolar macrophage hyerplasia was observed in 3 of 22 sham-exposed rats and 1 of 22 rats exposed to 0.32 mg Cu-Zn/m^3. Neither type II pneumocyte hyperplasia nor alveolitis was observed at the end of exposure in sham-exposed rats or rats exposed to 0.32 or 1.0 mg Cu-Zn/m^3; after the 4-week recovery period, alveolar macrophage hyperplasia was again not seen in

sham-exposed rats, but was seen in 1 of 22 rats exposed to 0.32 or 1.0 mg Cu-Zn/m^3. Also, after the recovery period, 1 of 22 rats exposed to 0.32 mg Cu-Zn/m^3 had evidence of a slight degree of alveolitis, but none of the sham-exposed rats or rats exposed to 1.0 mg Cu-Zn/m^3 had the lesion. All of these lesions in rats exposed to less than 3.2 mg Cu-Zn/m^3 had a slight severity rating, and with the exception of the nasal epithelial atrophy produced by exposure to 1.0 mg Cu-Zn/m^3, and were not observed at the end of the 13-week exposure period. Therefore, they did not appear to represent adverse biological responses to inhaled Cu-Zn alloy powder.

This study was conducted with F344/N rats to provide data to help predict the consequences of human inhalation exposures to this metal powder. It is reasonable to assume that the same or similar biological effects would be produced in the same target tissues and organs of rats and humans if the exposures of those anatomical structures were similar. Using available information about differences in the deposition of inhaled materials in the respiratory tracts of rats and humans (Schlesinger, 1985; Snipes, 1988), it is possible to estimate the relative exposure conditions needed to produce the same or similar tissue exposures and biological effects in rats and humans exposed to powdered Cu-Zn alloy. Since the Cu-Zn alloy powder clears very rapidly from the respiratory tract, this estimate does not include known differences between rats and humans in the rates of physical clearance of materials after their deposition in the respiratory tract. The assumption was made that the amount of deposited Cu-Zn dictates the type and magnitude of biological responses to the inhaled Cu-Zn.

The respiratory minute volume of F344/N rats is about 0.2 L; the minute respiratory volume of humans involved in "light activity" is about 20 L. Per

kilogram body weight, rats have minute respiratory volumes about 2.8 times greater than humans. In addition, regional deposition patterns result in markedly different exposure patterns for materials inhaled by rats and humans. Rats are obligatory nose-breathers, whereas humans breathe through their mouths or noses. Mouth-breathing humans would have a total deposition of about 50 percent (Morrow et al., 1966) of the Cu-Zn alloy aerosols used in this project, with most of the deposition in the pulmonary region. Nose-breathing humans would also deposit about 50 percent of the inhaled aerosol in the respiratory tract, but the deposition would be about equally divided between the upper respiratory tract and the pulmonary region. Rats would deposit about 40 percent of the inhaled material in the upper respiratory tract and about 5 to 10 percent of the material in the pulmonary region. Therefore, rats breathing an aerosol containing 1 mg Cu-Zn/m^3 would be expected to deposit about 0.01 to 0.02 μg Cu-Zn/minute in a 1.5 gram lung (0.007 to 0.013 μg Cu-Zn/g lung/minute). Mouth-breathing humans would deposit about 10 μg of Cu-Zn/minute in a 1000 gram lung (0.010 μg Cu-Zn/g lung/minute); and nose-breathing humans would deposit about 0.05 μg Cu-Zn/g lung/minute and about 5 μg Cu-Zn/minute in the upper respiratory tract. Because of the species differences in respiratory minute volume, fractional pulmonary deposition, and lung size, rats would have pulmonary deposition (μg Cu-Zn/g lung) comparable to that of mouth-breathing humans and about twice as high as that of nose-breathing humans.

While pulmonary deposition (μg Cu-Zn/g lung/minute) for the same aerosol of Cu-Zn would be similar for rats and humans, deposition in the upper respiratory tract would be quite different. A rat with a respiratory minute volume of 0.2 L, breathing an aerosol containing 1 mg Cu-Zn/m^3, would deposit

about 40 percent of the inhaled Cu-Zn (0.4 μg/minute) in the upper respiratory tract. A nose-breathing human would deposit about 5 μg/minute in the upper respiratory tract. Scaling the body weights of humans (70 kg) to body weights of rats (0.25 kg), and assuming the weights of nasal epithelium scale accordingly, the relative deposition of Cu-Zn in the rat's nasal epithelium could be about 20 times higher than for humans.

These comparisons for pulmonary and upper respiratory tract deposition of inhaled Cu-Zn alloy suggest that comparable exposures of the pulmonary region would result in rats and humans exposed to the same aerosol of powdered Cu-Zn alloy. The exposure of the tissues of the upper respiratory tract was estimated to be about 20 times higher for rats than for humans exposed to the same aerosol. Therefore, while lesions seen in the pulmonary region in this project might be similar for rats and humans exposed to the same aerosol of powdered Cu-Zn alloy, aerosol concentrations of Cu-Zn alloy would have to be much higher for human exposures to produce the same effects in the upper respiratory tracts as were observed in the F344/N rats.

VIII. NO OBSERVABLE ADVERSE EFFECTS LEVEL OF EXPOSURE

The no observable adverse effects level of exposure, for F344/N rats exposed to this respirable powder of Cu-Zn, is concluded on the basis of results of these studies to be an exposure equivalent to 0.32 mg Cu-Zn/m^3, 1.5 hours/day, 4 days/week.

IX. QUALITY ASSURANCE STATEMENT

Test Chemical: Cu-Zn Alloy Powder

Study Type: Phase III: Subchronic Inhalation Exposures in F344/N Rats

This research was conducted in accordance with the Good Laboratory Practice Regulations for Nonclinical Laboratory Studies (FDA, 1978). The study phases were inspected by the LITRI Quality Assurance Unit and findings reported to study scientists and to LITRI management. The final report is in accordance to the experimental methods described in study protocols and in standard operating procedures.

Documentation records, raw data, and pathology specimens pertaining to this study shall be archived and retained at the LITRI in accordance with 21 CFR Part 58 Good Laboratory Practice for Nonclinical Laboratory Studies.

QA Unit Schedule

Experimental Phase	Inspection Date	Report Date
Protocol FY86-016 Audit	04/02/86	04/02/86
Protocol FY86-016 Approval	06/09/86	06/09/86
Path/Tox Protocol Approval	06/10/86	N/A
Animal Quarantine Room	06/24/86	06/30/86
Facility Clin Path Lab	07/08/86	07/15/86
Exposure Room Prestudy	06/24/86	06/30/86
Exposure Room (Dosing)	07/10/86	07/30/86
Animal Weighing/Observations	07/24/86	07/30/86
Necropsy	09/23/86	09/23/86
Protocol FY87-009 Audit	11/21/86	11/21/86
Protocol FY87-009 Approval	01/22/87	01/22/87
Path/Tox Protocol Approval	01/13/87	N/A
Animal Quarantine/Weights	01/14/87	01/30/87
Exposure Room (Dosing)	02/18/87	02/28/87
Animal Weighing/Observations	03/12/87	03/12/87
Necropsy	04/29/87	04/30/87
	05/27/87	05/27/87

QA Unit Schedule (Cont.)

Experimental Phase	Inspection Date	Report Date
Data Audit	12/10-11/87	12/31/87
Data Audit	02/04-09/88	02/10/88
Final Report Data Audit	06/16-20/88	06/20/88
Final Report Audit	06/20/88	06/20/88

LITRI Quality Assurance Officer: D L Harris 8-1-88

D. L. Harris

LITRI Study Director: Morris B Snipes 8/1/88

M. B. Snipes, Ph.D.

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XII. APPENDICES

A. Explanation of Symbols and Abbreviations.

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C. Body Weights (Grams) for Individual Animals.

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J. Miscellaneous.

APPENDIX A: EXPLANATION OF SYMBOLS AND ABBREVIATIONS

(Defined in alphabetical order)

1. AFC = Antibody-forming cells per million lymphocytes in lung-associated lymph nodes.

2. AIRC = Airway collagen expressed as micrograms present in the lavage fluid.

3. ALB = Albumin in grams/dL serum.

4. ALKP = Alkaline phosphatase activity in international units/L serum.

5. ALKPL = Alkaline phosphatase in lung lavage fluid; milli-international units.

6. Animal Number = Animal number. Metal eartags were used in this study for permanent animal identification.

7. Assign Code = Assignment code, indicating the fate of the animals used in this study.

   EOE = Animals killed for endpoint evaluations after the exposure period.

   REC = Animals killed for endpoint evaluations after the recovery period following aerosol exposures.

8. BGLUL = Beta glucuronidase in lung lavage fluid; milli-international units.

9. BWBC = Leukocyte (WBC) numbers per mm^3 of blood.

10. BUN = Blood urea nitrogen in milligrams/dL serum.

11. CCORD = Quasistatic cord compliance (mL per cm water).

12. CDYN = Dynamic lung compliance (mL per cm of water).

13. DLCO = Carbon monoxide diffusing capacity (mL per minute per millimeter of mercury).

14. EA/100 Cells = Number of opsonized sheep red blood cells (SRBC) phagocytized per 100 pulmonary alveolar macrophages.

15. EF10 = Forced expiratory flow rate at 10 percent of FVC (mL per second).

16. EOSI = Eosinophils in blood, expressed as numbers of eosinophils per 100 leukocytes.

17. Exposure Code:

SHAM - Exposures of rats to humidified, filtered air using the same kind of nose-only exposure system as used for the Cu-Zn alloy powder. Exposures were 1.5 hr/day, 4 days/week.

Other exposure groups are expressed as mg Cu-Zn/m3 to indicate the exposure atmosphere they breathed.

18. Expt Number = LITRI experiment number.

19. FEV1 = Percent of FVC exhaled in 0.1 second.

20. FRC = Functional residual capacity (mL).

21. FVC = Forced vital capacity (mL).

22. HEMA = Hematocrit = The percentage ratio of volume of packed cells to red blood cells volume of whole blood.

23. HGB = Hemoglobin levels in blood, expressed as grams per dL of blood.

24. Histopathology codes:

0 = No changes relative to normal; lesion not present.
1 = Slight degree of change, or small amount present; mild response.
2 = Moderate, median, or middle severity or amount.
3 = Marked severity or degree of change, large amount present.

25. LDHL = Lactic dehydrogenase in lung lavage fluid; milli-international units.

26. LYMP = Lymphocytes in blood, expressed as numbers of lymphocytes per 100 leukocytes.

27. MCHV = Mean corpuscular hemoglobin concentration. The average concentration of hemoglobin in red blood cells in percent.

28. MCV = Mean corpuscular volume. The average volume of red blood cells in units of cubic micrometers.

29. MMEF = Mean mid-expiratory flow rate (mL per second).

30. MONO = Monocytes in blood, expressed as numbers of monocytes per 100 leukocytes.

31. MV = Minute volume (mL per minute).

32. NCELL = Total cells in centrifuge pellet from lavage fluid.

33. NEA = Number of erythrocytes phagocytized by 100 pulmonary alveolar macrophages.

34. NEOS = Total number of eosinophils in lavage fluid.

35. NLYM = Total number of lymphocytes in lavage fluid.

36. NMAC = Total number of macrophages in lavage fluid.

37. NPMN = Total number of neutrophils in lavage fluid.

38. NRBC = Nucleated erythrocytes per 100 leukocytes in blood.

39. PAMN = Pulmonary alveolar macrophages per mm^3 of lavage fluid.

40. PEFR = Peak expiratory flow rate (mL per second).

41. PEOS = Percentage of cells in lavage fluid that were eosinophils.

42. PLYM = Percentage of cells in lavage fluid that were lymphocytes.

43. PMAC = Percentage of cells in lavage fluid that were macrophages.

44. PMNN = Polymorphonuclear leukocytes per mm^3 of lavage fluid.

45. PPAM = Percentage of pulmonary alveolar macrophages that phagocytized one or more erythrocytes.

46. PPMN = Percentage of cells in lavage fluid that were neutrophils.

47. RBC = Erythrocytes (RBC) per mm^3 of blood.

48. RL = Total pulmonary resistance (cm water per mL per second).

49. RV = Residual volume (mL).

50. SBWT = Body weights of rats at the time they were killed for endpoint evaluations.

51. SEGM = Segmenter (neutrophil) levels in blood, expressed as numbers of neutrophils per 100 leukocytes.

52. SGPT = Serum glutamic pyruvic transaminase (alanine aminotransferase) activity in international units/L serum.

53. SIII = Slope of Phase III of a single-breath nitrogen washout (percentage of nitrogen per mL).

54. TBIL = Total bilirubin in milligrams/dL serum.

55. TLC = total lung capacity (mL).

56. Total AFC = Total IgM anti-SRBC antibody-forming cells in lung-associated lymph nodes.

57. Total Cells = Number of lymphoid cells in lung-associated lymph nodes ($x\ 10^{-6}$).

58. TPROL = Milligrams of protein in lung lavage fluid.

59. TPRO = Total serum protein in grams/dL serum.

60. VC = Vital capacity (mL).

61. WBCN = White blood cells per mm^3 of lavage fluid ($x\ 10^{-3}$).

APPENDIX B: DAILY AEROSOL CONCENTRATIONS OF Cu-Zn ALLOY POWDER

EXPOSURE DATE	EXPERIMENT NUMBER	Cu-Zn ALLOY CONCENTRATION (mg/m3)	NUMBER OF FILTERS	SAMPLING TIME (Minutes)
6-30-86	4371	0.907	3	90
7-01-86	4371	1.075	2	90
7-02-86	4371	1.103	4	90
7-03-86	4371	0.879	4	90
7-07-86	4371	1.083	4	90
7-08-86	4371	0.903	4	90
7-09-86	4371	1.111	4	90
7-10-86	4371	1.176	4	90
7-14-86	4371	1.195	4	90
7-15-86	4371	1.095	4	90
7-16-86	4371	1.334	4	90
7-17-86	4371	1.086	4	90
7-21-86	4371	1.121	4	90
7-22-86	4371	1.001	4	90
7-23-86	4371	0.928	3	90
7-24-86	4371	1.153	3	90
7-28-86	4371	1.073	4	90
7-29-86	4371	0.952	4	90
7-30-86	4371	1.035	4	90
7-31-86	4371	0.987	4	90
8-04-86	4371	1.029	4	90
8-05-86	4371	0.934	3	90
8-06-86	4371	1.033	4	90
8-07-86	4371	0.819	4	90
8-11-86	4371	0.915	4	90
8-12-86	4371	1.133	4	90
8-13-86	4371	0.954	4	90
8-14-86	4371	0.802	4	90
8-15-86	4371	1.142	4	90
8-18-86	4371	0.914	4	90
8-19-86	4371	0.826	4	90
8-20-86	4371	1.059	4	90
8-21-86	4371	0.953	4	90
8-25-86	4371	1.059	4	90
8-26-86	4371	1.074	4	90
8-27-86	4371	1.051	4	90
8-28-86	4371	1.021	3	90
9-02-86	4371	1.046	4	90
9-03-86	4371	1.230	4	90
9-04-86	4371	1.076	4	90
9-05-86	4371	1.076	4	90
9-08-86	4371	1.001	4	90
9-09-86	4371	0.989	3	90
9-10-86	4371	0.915	4	90
9-11-86	4371	0.978	4	90

EXPOSURE DATE	EXPERIMENT NUMBER	Cu-Zn ALLOY CONCENTRATION (mg/m3)	NUMBER OF FILTERS	SAMPLING TIME (Minutes)
9-15-86	4371	1.109	4	90
9-16-86	4371	0.983	4	90
9-17-86	4371	1.175	4	90
9-18-86	4371	1.061	4	90
9-22-86	4371	1.023	4	90
9-23-86	4371	0.994	4	90
9-24-86	4371	1.126	4	90
9-25-86	4371	0.922	4	90
6-30-86	4372	3.256	4	90
7-01-86	4372	3.456	4	90
7-02-86	4372	3.273	4	90
7-03-86	4372	2.559	4	90
7-07-86	4372	3.566	4	90
7-08-86	4372	3.483	4	90
7-09-86	4372	2.992	4	60
7-10-86	4372	3.230	4	90
7-14-86	4372	3.727	4	90
7-15-86	4372	3.366	4	90
7-16-86	4372	3.190	4	90
7-17-86	4372	2.994	4	90
7-21-86	4372	3.834	4	90
7-22-86	4372	3.198	4	90
7-23-86	4372	3.431	4	90
7-24-86	4372	2.851	4	90
7-28-86	4372	3.366	4	90
7-29-86	4372	3.326	4	90
7-30-86	4372	3.016	4	90
7-31-86	4372	2.685	4	90
8-04-86	4372	3.175	4	90
8-05-86	4372	3.600	4	90
8-06-86	4372	3.218	4	90
8-07-86	4372	3.154	3	90
8-11-86	4372	3.646	4	90
8-12-86	4372	4.050	4	90
8-13-86	4372	3.195	4	90
8-14-86	4372	3.350	3	90
8-15-86	4372	3.325	4	90
8-18-86	4372	2.797	3	90
8-19-86	4372	4.160	4	90
8-20-86	4372	3.236	3	90
8-21-86	4372	3.079	4	90
8-25-86	4372	3.108	3	90
8-26-86	4372	2.966	4	90
8-27-86	4372	3.663	4	90

EXPOSURE DATE	EXPERIMENT NUMBER	Cu-Zn ALLOY CONCENTRATION (mg/m3)	NUMBER OF FILTERS	SAMPLING TIME (Minutes)
8-28-86	4372	3.367	3	90
9-02-86	4372	2.922	4	90
9-03-86	4372	3.311	4	90
9-04-86	4372	3.563	4	90
9-05-86	4372	3.376	4	90
9-08-86	4372	3.659	4	90
9-09-86	4372	3.249	3	90
9-10-86	4372	3.190	4	90
9-11-86	4372	3.459	4	90
9-15-86	4372	4.145	4	90
9-16-86	4372	3.134	4	90
9-17-86	4372	3.858	4	90
9-18-86	4372	3.066	4	90
9-22-86	4372	3.391	4	90
9-23-86	4372	3.210	4	90
9-24-86	4372	3.125	4	90
9-25-86	4372	3.661	4	90
6-30-86	4373	6.570	4	90
7-01-86	4373	9.882	4	90
7-02-86	4373	7.841	4	90
7-03-86	4373	10.754	4	90
7-07-86	4373	10.638	4	90
7-08-86	4373	10.580	4	90
7-09-86	4373	10.086	4	90
7-10-86	4373	10.664	4	90
7-14-86	4373	8.842	4	90
7-15-86	4373	10.357	4	90
7-16-86	4373	10.379	4	90
7-17-86	4373	11.296	4	90
7-21-86	4373	10.772	4	90
7-22-86	4373	10.382	4	90
7-23-86	4373	11.864	4	90
7-24-86	4373	8.642	4	90
7-28-86	4373	10.057	4	90
7-29-86	4373	8.909	4	90
7-30-86	4373	10.820	4	90
7-31-86	4373	10.944	4	90
8-04-86	4373	13.748	4	90
8-05-86	4373	12.665	4	90
8-06-86	4373	13.030	4	90
8-07-86	4373	11.019	4	90
8-11-86	4373	8.286	4	90
8-12-86	4373	11.951	4	90
8-13-86	4373	8.609	4	90
8-14-86	4373	9.706	4	90

EXPOSURE DATE	EXPERIMENT NUMBER	Cu-Zn ALLOY CONCENTRATION (mg/m3)	NUMBER OF FILTERS	SAMPLING TIME (Minutes)
8-15-86	4373	10.191	4	90
8-18-86	4373	12.127	4	90
8-19-86	4373	9.242	4	90
8-20-86	4373	8.954	4	90
8-21-86	4373	9.241	3	90
8-25-86	4373	11.740	4	90
8-26-86	4373	10.160	4	90
8-27-86	4373	8.039	3	90
8-28-86	4373	10.308	4	90
9-02-86	4373	8.983	4	90
9-03-86	4373	10.929	4	90
9-04-86	4373	9.247	3	90
9-05-86	4373	10.046	4	90
9-08-86	4373	10.845	4	90
9-09-86	4373	10.359	4	90
9-10-86	4373	10.564	4	90
9-11-86	4373	8.964	3	90
9-15-86	4373	10.006	4	90
9-16-86	4373	10.863	3	90
9-17-86	4373	10.514	4	90
9-18-86	4373	10.267	4	90
9-22-86	4373	10.637	4	90
9-23-86	4373	10.573	3	90
9-24-86	4373	10.341	4	90
9-25-86	4373	9.997	4	90
1-27-87	4443	0.445	4	90
1-28-87	4443	0.181	4	90
1-29-87	4443	0.313	3	90
1-30-87	4443	0.325	3	90
2-02-87	4443	0.319	3	90
2-03-87	4443	0.294	3	90
2-04-87	4443	0.329	4	90
2-05-87	4443	0.330	4	90
2-09-87	4443	0.287	3	90
2-10-87	4443	0.308	4	90
2-11-87	4443	0.336	4	90
2-12-87	4443	0.316	4	90
2-17-87	4443	0.297	4	90
2-18-87	4443	0.317	4	90
2-19-87	4443	0.316	4	90
2-20-87	4443	0.309	3	90
2-23-87	4443	0.230	3	90
2-24-87	4443	0.399	4	90
2-25-87	4443	0.373	4	90
2-26-87	4443	0.300	3	90

EXPOSURE DATE	EXPERIMENT NUMBER	Cu-Zn ALLOY CONCENTRATION (mg/m3)	NUMBER OF FILTERS	SAMPLING TIME (Minutes)
3-02-87	4443	0.283	4	90
3-03-87	4443	0.358	4	90
3-04-87	4443	0.376	4	90
3-05-87	4443	0.360	4	90
3-09-87	4443	0.297	4	90
3-10-87	4443	0.364	4	90
3-11-87	4443	0.348	4	90
3-12-87	4443	0.335	4	90
3-16-87	4443	0.365	4	90
3-17-87	4443	0.336	4	90
3-18-87	4443	0.317	3	90
3-19-87	4443	0.306	4	90
3-23-87	4443	0.261	4	90
3-24-87	4443	0.321	4	90
3-25-87	4443	0.322	4	90
3-26-87	4443	0.318	4	90
3-30-87	4443	0.306	3	90
3-31-87	4443	0.271	4	90
4-01-87	4443	0.312	3	90
4-02-87	4443	0.317	4	90
4-06-87	4443	0.335	4	90
4-07-87	4443	0.330	4	90
4-08-87	4443	0.314	4	90
4-09-87	4443	0.287	4	90
4-13-87	4443	0.268	4	90
4-14-87	4443	0.297	4	90
4-15-87	4443	0.309	4	90
4-16-87	4443	0.271	3	90
4-20-87	4443	0.322	4	90
4-21-87	4443	0.326	4	90
4-22-87	4443	0.306	4	90
4-23-87	4443	0.358	4	90
1-27-87	4444	3.999	4	90
1-28-87	4444	3.618	4	90
1-29-87	4444	3.158	4	90
1-30-87	4444	3.047	4	90
2-02-87	4444	3.743	4	90
2-03-87	4444	3.450	4	90
2-04-87	4444	3.143	4	90
2-05-87	4444	3.099	4	90
2-09-87	4444	2.570	4	90
2-10-87	4444	2.960	4	90
2-11-87	4444	3.715	4	90
2-12-87	4444	3.722	4	90
2-17-87	4444	3.375	4	90

EXPOSURE DATE	EXPERIMENT NUMBER	Cu-Zn ALLOY CONCENTRATION (mg/m3)	NUMBER OF FILTERS	SAMPLING TIME (Minutes)
2-18-87	4444	3.155	4	90
2-19-87	4444	3.072	4	90
2-20-87	4444	3.002	4	90
2-23-87	4444	3.119	3	90
2-24-87	4444	3.217	4	90
2-25-87	4444	3.909	3	90
2-26-87	4444	2.459	4	90
3-02-87	4444	3.099	4	90
3-03-87	4444	3.477	4	90
3-04-87	4444	3.360	4	90
3-05-87	4444	3.085	4	90
3-09-87	4444	3.347	4	75
3-10-87	4444	3.341	4	90
3-11-87	4444	2.574	4	90
3-12-87	4444	2.982	4	90
3-13-87	4444	3.274	3	90
3-16-87	4444	3.440	4	90
3-17-87	4444	3.585	4	90
3-18-87	4444	2.614	4	90
3-19-87	4444	4.023	4	90
3-23-87	4444	3.795	4	90
3-24-87	4444	3.650	4	90
3-25-87	4444	3.445	4	90
3-26-87	4444	3.200	4	90
3-30-87	4444	3.433	4	90
3-31-87	4444	3.307	4	90
4-01-87	4444	2.431	4	90
4-02-87	4444	3.553	4	90
4-06-87	4444	2.937	4	90
4-07-87	4444	3.120	3	90
4-08-87	4444	2.748	4	90
4-09-87	4444	2.896	4	90
4-13-87	4444	2.917	4	90
4-14-87	4444	2.735	4	90
4-15-87	4444	3.687	4	90
4-16-87	4444	3.041	4	90
4-20-87	4444	2.429	4	90
4-21-87	4444	3.208	4	90
4-22-87	4444	3.645	4	90
4-23-87	4444	3.617	4	90

APPENDIX C: BODY WEIGHTS (GRAMS) FOR INDIVIDUAL ANIMALS

PHASE III, PART 1 ----- BODY WEIGHT IN GRAMS ON STUDY DAY:

EXPT	ANI	SEX	-1	3	6	10	13	17	20	24	27	31	32	34	38	41	45	48	52	55	59	62	66	69	73	78	80	83	87
4370	001	M	297	290	289	292	295	295	298	297	290	300		303	307	308	305	308	305	310	305	309	305	302	310	308	306	314	
4370	002	M	295	293	290	291	295	297	294	300	294	302		299	306	309	308	311	313	317	316	316	318	316	321		319	326	
4370	003	M	275	272	273	276	279	277	275	279	273	283		281	288	292	284	283	293	292	298	299	302	297	305	303	307	312	
4370	004	M	270	266	268	269	271	272	271	272	267	272		274	275	278	271	275	281	278	278	278	276	274	280	283	278	287	
4370	005	M	282	277	277	278	281	281	278	291	281	282		286	291	292	287	293	296	297	294	296	289	287	292	294	285	296	
4370	006	M	289	285	288	288	290	288	289	284	285	290		293	292	292	294	295	298	297	299	295	297	291	298	302	301	308	
4370	007	M	284	283	285	285	285	286	286	284	280	289		286	292	295	286	290	293	296	296	297	296	291	301	301	300	309	
4370	008	M	263	264	264	266	269	271	271	272	273	277		275	284	285	286	287	289	293	296	296	297	288	300	304	305	305	
4370	009	M	272	271	270	269	273	275	274	278	273	279		282	283	289	286	289	296	295	298	291	298	289	299	297	297	304	
4370	010	M	286	284		285	289	290	290	294	291	296		294	302	306	305	297	306	305	309	313	311	304	315	316	314	317	
4370	011	M	271	270	270	270	272	273	272	273	267	275		277	282	284	282	283	288	287	295	293	291	288	298	299	296	304	
4370	012	M	269	261	263	261	264	262	263	261	259	265		266	268	270	268	270	272	274	277	277	274	271	279	279	279	288	
4370	013	M	274	271	265	267	271	271	273	276	273	277		277	282	289	287	291	293	301	300	299	301	297	307	309	307	314	
4370	014	M	274	271	270	269	273	271	273	279	279	284		284	290	293	290	290	295	292	301	299	300	298	311	307	306	312	
4370	015	M	297	295	299	299	304	303	305	307	303	310		305	312	311	309	312	315	318	319	320	315	312	315	318		322	
4370	016	M	277	276	276	276	277	281	282	286	282	294		289	299	298	297	301	308	308	305	302	303	298	305	306		311	
4370	017	M	274	273	276	274	277	277	274	279	276	278		279	281	279	277	277	283	282	285	283	285	284	290	290	289	295	
4370	018	M	281	278	281	279	282	284	286	288	286	289		292	297	295	293	295	303	303	304	300	300	295	304	302	301	303	
4370	019	M	276	273	273	273	274	275	279	279	280	283		283	287	288	286	285	282	272	282	284	287	285	293	296	294	301	
4370	020	M	272	273	271	275	279	280	282	282	280	284		282	287	286	281	287	290	290	295	292	291	285	294	295	293	299	
4370	021	M	278	277	274	280	282	288	289	295	297	287		298	303	307	303	302	309	306	316	314	316	313	319	317	320	325	
4370	022	M	272	268	270	273	277	276	277	280	280			283	289	295	298	295	304	303	306	305	304	303	313	312	315	319	
4370	023	M	296	295	296	295	295	299	301	307	303	306		306	311	314	306	308	314	314	319	319	320	315	325	324	324	328	
4370	024	M	274	270	270	269	272	273	272	276	273	279		280	279	284	279	285	285	286	290	286	287	285	290	291	293	299	
4370	025	M	273	269		262	271	278	281	284	281	285		287	289	292	289	288	294	292	297	295	292	288	296	299	295	304	
4370	026	M	266	263	264	265	269	274	271	273	274	274		274	277	280	276	276	283	280	287	282	279	273	284	290	288	293	
4370	027	M	271	267	272	272	278	279	282	283	279	286		280	286	288	283	282	291	296	298	296	297	292	302	304	300	307	
4370	028	M	271	262	266	266	270	273	275	280	278	284		286	290	289	287	288	293	295	295	288	291	283	296	297	293	301	
4370	029	M	277	275	275	278	282	284	287	288	288	290		293	290	291	290	292	297	299	300	298	297	294	299	303	298	306	
4370	030	M	291	288	289	287	289	290	292	295	299	300		304	304	305	304	303	312	310	310	306	310	305	312	316	311	320	
4370	031	M	280	270	273	273	279	283	283	288	287	289		288	291	293	291	294	300	298	303	300	303	296	306	305	304	310	
4370	032	M	286	279	280	278	281	284	286	287	285	288		288	293	294	294	294	302	301	304	302	299	295	303	304	305	309	
4370	033	M	295	285	288	289	295	297	296	300	301	305		301	306	312	308	317	314	311	313	318	317	318	320	326	322	329	
4370	034	M	0	285	286	287	291	293	291	292	293	296		291	297	302	298	302	308	305	312	311	313	308	313	320	321	324	
4370	035	M	268	261	258	263	265	267	267	272	269	275		272	280	287	283	285	287	285	285	285	285	285	287	289	283	288	
4370	036	M	279	280	279	277	277	280	280	281	281	283		279	288	289	289	289	294	297	299	299	300	294	303	304	299	305	

PHASE III, PART 1 ----- BODY WEIGHT IN GRAMS ON STUDY DAY:

EXPT	ANI	SEX	-1	3	6	10	13	17	20	24	27	31	32	34	38	41	45	48	52	55	59	62	66	69	73	76	80	83	87
4370	501	F	190	183	186		186	182	187	179	186	185		192	187	192	191	194	194	196	193	191	193	193	198	199	195	199	
4370	502	F	180	181	182		182	179	179	172	179	180		182	181	186	184	183	192	193	191	187	187	186	191	193	191	193	
4370	503	F	178	176	172		177	167	175	174	176	180		182	183	186	186	183	185	186	187	183	186	183	189	193	188	194	186
4370	504	F	172	171	167		171	173	166	164	171	174		178	181	183	183	180	185	184	189	186	185	185	192	196	189	193	
4370	505	F	174	174	171		170	173	170		173	176		177	177	177	177	181	180	181	182	181	179	177	184	183	182	184	
4370	506	F	172	173	168		170		157	157	169	174		168	166	175	178	179	180	181	181	180	181	176	182	184	181	186	
4370	507	F	166	163	164		163	163	163	160	163	164		176	166	170	168	171	173	178	176	175	174	169	176	177	176	177	
4370	508	F	175	171	173		174	178	176	167	173	177		178	185	186	186	184	187	187	191	187	189	183	190	187	188	191	
4370	509	F	175	172	171		171	170	168	165	169	176		173	178	178	179	182	186	185	187	181	182	180	182	188	185	190	
4370	510	F	177	173	176		174	175	173	172	175	179		179	186	187	184	186	188	189	188	189	189	188	192	194	189	196	
4370	511	F	180	172	174		177	171	173	171	180	182		184	184	186	186	188	191	188	187	189	189	187	192	193	190	196	184
4370	512	F	166	161	164		162	164	164	157	161	168		167	172	170	170	170	174	174	174	173	172	169	175	175	172	176	
4370	513	F	168	169	166		170	172	168	167	167	175		175	176	175	174	173	180	179	181	180	176	177	181	184	181	183	
4370	514	F	174	175	173		174	176	174	171	177	182		184	185	184	183	183	187	185	187	187	187	185	188	189	186	190	184
4370	515	F	184	170	178		176	180	177	173	178	179		181	183	184	187	188	192	192	192	191	191	18	194	193	189	197	
4370	516	F	177	174	175		174	169	172	164	171	171		177	177	180	180	181	183	179	184	182	183	179	184	188	186	187	
4370	517	F	172	168	170		174	175	174	167	173	176		176	177	174	178	177	182	176	184	182	180	176	183	186	183	186	
4370	518	F	187	183	183		184	185	184	178	187	187		190	193	195	194	192	196	192	194	196	193	188	195	197	193	196	
4370	519	F	168	169	172		173	173	174	170	178	180		182	182	186	184	181	185	186	188	189	187	186	191	197	193	195	
4370	520	F	172	172	172		173	167	170	163	171	173		173	177	177	177	178	182	179	184	183	181	186	183	184	178	185	
4370	521	F	184	182	184		186	183	179	180	184	186		189	193	193	191	186	196	195	197	196	194	186	195	199	195	199	
4370	522	F	177	178	172		177	181	174	168	173	178		182	182	178	177	170	178	178	181	180	179	175	183	183	179	181	
4370	523	F	175	173	173		169	171	165	167	171	170		173	177	174	175	173	176	177	180	179	177	172	179	183	179	182	
4370	524	F	171	170	167		169	164	166	166	166	171		172	173	174	172	170	175	174	178	178	175	174	178	178	176	179	
4370	525	F	172	168	168		167	163	164	166	172	176		178	177	182	180	177	182	182	188	183	186	181	186	188	186	189	
4370	526	F	165	165	162		163	165	164	162	165	169		170	169	171	168	167	174	171	176	175	177	174	181	185	180	184	
4370	527	F	175	170	174		172	169	172	167	171	173		178	176	178	176	178	182	178	182	181	180	179	180	186	179	185	
4370	528	F	168	162	163		167	161	164	159	167	170		174	174	175	172	171	177	174	177	177	176	179	176	177	174	179	
4370	529	F	172	166	169		171	170	170	158	168	167		173	175	177	176	175	178	178	177	178	178	176	182	182	180	183	
4370	530	F	177	172	167		175	171	172	169	177	177		178	180	185	183	177	183	186	185	184	185	183	188	187	184	189	
4370	531	F	178	174	174		173	172	171	168	174	175		177	176	177	176	180	182	181	186	182	185	182	185		179	187	
4370	632	F	182	179	180		178	179	176	172	177	181		186	186	189	188	181	188	186	192	188	188	182	192			191	
4370	533	F	176	171	171		175	172	173	161	169	170		175	177	183	179	178	184	180	187	186	184	182	186	190	186	192	
4370	534	F	168	165	167		170	171	169	167	169	174		176	176	178	176	176	182	180	184	183	181	179	183	183	183	185	
4370	535	F	174	171	164	161	170	170	169	166	169	169		174	172	173	176	174	182	180	182	177	177	174	179	183	178	185	
4370	536	F	174	172	173		172	173	174	168	171	172		178	175	178	176	175	180	180	180	183	179	174	182	185	183	186	
4371	037	M	302	287	289	288	292	294	297	296	298	302		295	302	306	303	302	308	307	311	307	309	304	311	318	316	321	317
4371	038	M	289	283	285		286	289	289	294	295	296		300	302	306	304	306	306	307	314	311	314	308	315	320	315	321	320
4371	039	M	282	281	280	278	283	283	285	284	285	286		289	285	293	291	292	294	297	297	295	298	296	300	307	301	308	305
4371	040	M	269	265	269	267	269	271	267	267	266	267		270		270	270	270	271	271	274	272	274	267	278	278	277	286	279

PHASE III, PART 1 ----- BODY WEIGHT IN GRAMS ON STUDY DAY:

EXPT	ANI	SEX	-1	3	6	10	13	17	20	24	27	31	32	34	38	41	45	48	52	55	59	62	66	69	73	76	80	83	87
4371	041	M	276	275	278	278	278	282	283	286	287	288		290	291	299	291	295	295	301	302	301	305	298	306	308	305	316	307
4371	042	M	287	282	281	279	284	286	290	292	290	289		290		301	295	303	299	300	300	304	302	294	305	303	307	316	313
4371	043	M	289	285	283	283	285	285	284	292	289	292		295		303	300	305	306	305	312	310	307	303	312	318	311		305
4371	044	M	266	264	264	262	264	265	265	267	266	268		272		280	276	277	281	284	284	282	288	281	291	296	295	300	295
4371	045	M	276	273	274	274	277	278	273	278	277	277		280	281	285	281	287	288	291	291	284	286	279	289	291	287	296	289
4371	046	M	297	295	294	295	296	300	297	301	292	301		298	304	313	311	313	318	313	319	312	320	314	324	317	323		332
4371	047	M	274	269	270	273	274	274	275	278	275	278		280	282	286	281	280	286	290	292	288	290	286	292	296	291	301	296
4371	048	M	271	270	267	265	266	270	269	272	271	272		270	277	281	274	276	280	277	284	282	282	279	281	281	282	287	284
4371	049	M	276	281	276	279	280	279	278	283	275	284		283	285	292	288	287	295	299	297	298	300	302	305	308	307	313	310
4371	050	M	286	287	287	286	289	289	290	296	295	299		297	297	303	297	304	305	307	308	308	307	303	310	308	312	320	316
4371	051	M	275	275	268	269	272	270	270	272	267	276		277	276	282	277	281	287	286	289	285	284	281	288	293	286	295	293
4371	052	M	275	272	271	270	272	271	274	270	271	273		272	275	281	280	281	286	286	284	287	285	282	288	293	286	294	289
4371	053	M	284	281	282	283	286	285	287	289	286	293		297	298	302	301	299	309	309	317	312	317	316	321	321	320	326	318
4371	054	M	277	272	273	270	270	268	273	275	275	277		281	278	283	279	284	285	286	289	290	293	288	292	294	292	301	290
4371	055	M	282	279	280	276	279	278	275	277	273	275		274	276	277	275	277	280	275	281	281	281	277	284	286	282	292	287
4371	056	M	284	280	281	278	284	280	283	287	287	287		291	290	296		297	297	296	299	297	296	294	297	299	296	306	301
4371	057	M	268	264	263	260	264	264	266	268	265	269		270	271	273	272	273	280	287	290	289	291	292	297	297	298	307	304
4371	058	M	274	271	271	271	273	273	274	275	270	275		276	276	279	275	279	285	285	289	285	284	282	289	292	289	294	288
4371	059	M	262	260	262	263	263	265	262	270	267	268		262	266	269	267	267	272	275	277	274	278	276	283	282	279	279	284
4371	060	M	298	291	291	289	290	291	294	294	292	294		296	292	298	293	297	296	302	301	303	300	297	301	300	297	306	303
4371	061	M	298	288	289	286	286	289	289	292	292	295		297	291	296	297	296	303	304	307	303	308	298	308	313	308	310	308
4371	062	M	272	270	271	268	270	275	275	273	272	272		274	269	274	274	278	276	279	278	279	277	269	275	278	274	279	278
4371	063	M	282	273	274	279	287	286	290	298	293	305		302	309	314	312	313	320	316	322	314	320	319	330	326	326	335	330
4371	065	M	277	278	275	275	280	281	279	279	275	279		277	275	280	277	285	285	286	288	289	288	286	292	294	289	292	290
4371	066	M	265	260	260	260	266	269	267	273	268	269		269	271	271	275	277	283	284	284	285	283	280	287	291	288	292	291
4371	067	M	287	285	285	285	287	289	285	296	294	297		299	298	302	303	305	306	306	311	309	311	313	315	318	314	323	320
4371	068	M	277	271	272	273	273	275	275	279	275	280		283	281	286	280	280	283	289	290	291	290	281	291	294	293	301	301
4371	069	M	284	276	278	280	280	286	288	288	287	286		284	286	293	288	289	293	295	297	296	294	293	300	307	302	312	306
4371	070	M	280	274	279	276	281	280	282	284	278	280		280	282	289	289	288	292	293	299	295	288	287	295	301	293	302	301
4371	071	M	277	259	254	256	261	266	267	268	270	268		270	274	278	277	275	283	286	286	287	285	287	293	294	290	297	298
4371	072	M	291	287	284	284	287	290	289	285	290	285		287	285	293	286	294	295	298	[illegible]	301	296	294	302	306	300	305	301
4371	073	M	284	282	280	278	278	282	283	284	283	285		286	287	295	291	298	297	290	[illegible]	299	300	295	303	310	307	315	309
4371	074	M	274	269	270	267	271	271	272	276	278	278		[illegible]	278	286	281	281	285	288	293	292	294	289	297	301	299	307	301
4371	537	F	181	180	180		180	181	178	174	179	180		183	183	185	182	179	184	181	186	185	183	180	186	188	185	186	184
4371	538	F	174	174	170		171	167	167																				
4371	539	F	186	182	180		180	177	176	169	175	173		178	178	180	179	180	184	183	186	184	184	182	186	190	189	191	187
4371	540	F	168	165	164		165	167	164	158	161	166		170	170	171	172	169	175	173	173	173	174	170	174	175	173	177	174
4371	541	F	172	171	168		174	172	167	164	168	167		173	177	177	176	175	181	179	183	181	181	179	183	186	182	187	186
4371	542	F	172	168	169		170	169	169	167	167	165		170	175	176	173	172	176	177	176	177	173	171	180	181	180	184	181
4371	543	F	166	159	157		160	159	156	152	154	152		158	162	163	162	160	166	162	166	165	164	176	164	166	164	167	165
4371	544	F	179	177	178		177	172	174	169	176	169		180	180	182	180	178	182	181	181	184	179	177	182	184	181	184	182

PHASE III, PART 1 ----- BODY WEIGHT IN GRAMS ON STUDY DAY:

EXPT	ANI	SEX	-1	3	6	10	13	17	20	24	27	31	32	34	38	41	45	48	52	55	59	62	66	69	73	76	80	83	87
4371	545	F	180	178	180		181	175	174	168	171	167		180	180	179	180	182	184	183	185	182	181	181	186	186	183	187	185
4371	546	F	177	178	181		179	182	177	174	177	174		181	182	181	181	179	184	185	184	185	185	182	188	188	187	195	188
4371	547	F	184	184	185		185	185	184	178	173	180		186	190	192	188	185	189	185	193	189	190	189	194	195	191	194	192
4371	548	F	172	167	168		168	165	166	168		165		175	179	177	178	175	183	184	182	177	182	176	184	184	182	187	186
4371	549	F	182	179	178		180	179	177	176	179	179		186	187	187	190	187	195	191	193	191	192	194	195	196	196	201	196
4371	550	F	178	176	175		177	176	177	171	178	173		181	182	183	183	182	187	184	186	185	181	185	187	188	186	186	185
4371	551	F	170	168	167		170	165	165	161	169	164		174	176	178	179	179	181	179	180	178	181	176	181	179	182	184	184
4371	552	F	183	182	179		183																						
4371	553	F	175	173	172		172	170	169	163	173	165		176	178	180	178	175	181	182	180	181	180	176	183	186	185	185	185
4371	564	F	176	173	173		172	172	173	166	171	166		178	175	178	175	178	180	182	182	181	178	184	184	187	186	186	184
4371	555	F	168	166	167		171	170	171	168	174	167		176	175	176	177	174	180	180	177	177	178	176	179	184	179	183	184
4371	556	F	180	176	174		175	175	176	170	172	169		178	178	180	178	176	181	180	184	181	181	175	181	184	182	188	189
4371	557	F	172	168	166		166	162	162	161	165	161		172	172	175	173	170	174	174	176	177	179	172	176	183	178	184	181
4371	558	F	182	175	177		179	180	180	175	176	172		184	185	185	187	186	186	187	196	190	190	185	192	195	189	198	194
4371	559	F	171	167	168		171	169	170	164		164		176	176	176		175	179	181	181	178	181	175	179	182	179	185	182
4371	560	F	188	183	182		184	185	183	179	168	178		189	192	193	190	186	192	190	195	190	190	183	189	189	193	198	195
4371	561	F	170	168	166		167	165	164	160	163	160		169	171	171	170	172	174	176	175	176	177	174	180	183	179	182	178
4371	562	F	159	157	156		156	154	154	146	152	152		159	164	164	163	165	166	165	169	164	168	163	167	168	168	169	170
4371	563	F	179	177	176		176	174	176	172	177		174	179	181	180	177	179	180	182	182	180	181	172	178	183	179	183	181
4371	564	F	178	174	176		176	172	173	169	177		176	182	179	183	182	179	185	184	187	186	186	182	186	188	186	190	187
4371	565	F	176	171	168	165	177	179	176	175	179		179	180	183	182	181	179	187	185	186	184	185	180	189	191	186	191	191
4371	566	F	170	169	174		169	168	166	167	168		166	169	171	174	170	170	173	175	178	175	176	168	176	175	174	179	175
4371	567	F	174	168	168		169	166	164	159	162		163	168	168	168	171	171	172	173	176	177	176	171	177	181	179	182	179
4371	568	F	181	177	176		178	173	168	165	173		171	179	178	180	182	177	181	179	184	185	184	179	188	190	182	190	186
4371	569	F	167	166	167		164	163	162	160	165		164	169	168	171	172	174	175	175	178	178	179	174	182	182	178	181	179
4371	570	F	172	169	170		168	168	166	162	167		173	179	176	180	177	177	180	176	182	178	180	172	181	182	179	186	178
4371	571	F	173	171	170		171	169	172	168	171		170	176	178	179	178		173	176	179	182	183	177	186	186	185	186	185
4371	572	F	168	160	162		165	159	160	157	163		162	167	166	170	163	163	169	166	170	169	172	168	172	161	169	175	175
4371	573	F	170	172	171		171	173	173	171	174		173	179	180	182	180	176	180	178	182	181	181	175	183	184	181	183	184
4371	574	F	170	170	169		168	170	168	164	165		170	173	177	174	176	175	180	175	182	173	176	175	183	184	181	185	180
4372	075	M	308	297	293	294	297	296	294	296	289	295		290	295	303	299	308	305		296	303	309	303	311	312	309	316	316
4372	076	M	296	291	289	290	292	294	291	293	294	298		299	300	295	304	306	308	307	308	306	312	308	316	316	313	323	313
4372	077	M	293	287	282	283	288	293	294	294	295	295		297	297	299	296	304	304	305	307	306	308	302	306	310	304	312	306
4372	078	M	281	272	277	273	277	279	281	286	284	286		288	289	290	285	294	292	290	294	289	295	290	299	301	299	306	295
4372	079	M	278	269	261		269	271	272	276	275	276		276	285	281	280	281	285	287	290	293	291	286	295	299	293	301	299
4372	080	M	293	289	283	285	285	282	284	285	284	285		286	289	288	290	297	297	302	306	305	303	302	310	313	310	316	311
4372	081	M	293	287	287	286	285	288	286	290	288	285		292	291	292	290	293	296	297	303	303	302	296	305	311	302	314	311
4372	082	M	270	262	264	266	267	269	269	270	266	269		273	271	278	274	269	280	281	285	278	286	279	291	289	291	294	295
4372	085	M	279	279	278	278	277	278	279	283	281	286		289	290	297	294	295	299	301	303	305	303	298	308	308	305	314	313
4372	086	M	290	284	286	286	286	287	287	291	286	291		291	292	296	293	299	297	300	307	305	302	299	306	309	304	309	306

PHASE III, PART I ----- BODY WEIGHT IN GRAMS ON STUDY DAY:

EXPT	ANI	SEX	-1	3	6	10	13	17	20	24	27	31	32	34	38	41	45	48	52	55	59	62	66	69	73	76	80	83	87
4372	087	M	297	294	293	294	293	294	295	298	293	296		293	296	298	298	311	310	313	312	316	311	308	317	321	314	329	324
4372	088	M	289	278	278	281	282	283	283	284	288	283		287	288	292	291	299	298	301	305	303	296	296	303	306	300	313	308
4372	089	M	292	262	261	263	263	262	263	268	270	271		271	278	283	279	285	283	285	289	286	288	284	293	297	291	300	295
4372	090	M	292	290	284	283	285	287	285	288	288	288		288	294	301	295	301	304	306	308	307	307	305	313	318	309	322	313
4372	091	M	287	276	277	278	281	279	279	279	282	285		281	289	292	285	291	295	300	297	300	299	298	300	306	301	310	304
4372	092	M	292	291	288	290	292	293	293	297	297	297		293	303	310	303	308	311	314	314	315	316	313	321	324	321	329	326
4372	093	M	273	268	265	266	269	270	272	275	276	281		284	287	289	289	293	294	292	298	297	295	290	300	302	297	306	304
4372	094	M	283	281	277	279	281	283	285	288	289	293		295	294	302	298	302	305	309	313	309	312	307	313	317	315	322	311
4372	095	M	272	271	270	272	251	261	266	279	267	276		268	276	275	275	278	285	281	286	281	286	282	288	292	290	299	294
4372	096	M	275	272	270		273	276	277	270	278	279		279	283	283	283	289	273	279	288	290	289	288	292	296	291	300	295
4372	097	M	262	264	263	264	264	267	267	272	269	272		273	273	277	273	279	279	280	283	283	281	276	285	290	286	293	287
4372	098	M	297	293	292	292	293	296	295	298	296	303		303	308	310	306	314	315	316	319	320	320	319	327	330	323	325	328
4372	099	M	284	278	275	277	280	280	282	281	282	286		285	287	288	289	295	292	298	297	299	299	297	303	307	302	310	301
4372	100	M	278	274	271		278	286	285	294	293	292		289	296	297	295	306	302	306	307	306	308	305	314	318	316	324	320
4372	101	M	280	276	273	272	274	273	279	276	280	284		287	291	290	290	295	299	301	300	301	304	299	306	308	304	306	305
4372	102	M	259	258	256	259	260	261	262	268	269	273		275	276	282	281	288	290	289	296	294	285	279	288	292	292	296	296
4372	103	M	276	270			268	267	269	269	268	270		268	269	275	269	274	275	278	276	277	276	273	280	283	279	289	283
4372	104	M	264	259	269		261	260	265	267	266	265		268	269	272	269	277	278	279	283	282	280	277	288	288	289	293	296
4372	105	M	279	265	264		275	279	281	284	285	288		289	290	293	293	292	297	301	302	303	305	299	311	314	310	315	317
4372	106	M	285	279	276	277	284	285	287	289	285	289		290	291	291	294	291	299	297	300	294	297	295	302	301	298	305	302
4372	107	M	278	273	273	275	279	278	281	283	285	286		286	289	290	288	296	299	300	297	295	294	289	293	302	296	303	303
4372	108	M	272	269	269	272	278	277	281	282	284	285		284	285	289	287	286	289	297	293	295	297	297	297	305	300	303	305
4372	109	M	284	278	273	275	288	280	280	286	285	288		282	285	287	287	286	291	289	294	290	294	289	299	302	296	301	298
4372	110	M	287	286	283	286	280	292	293	300	299	303		299	304	309	305	304	305	310	311	310	311	308	317	317	313	286	289
4372	111	M	289	283	279	278	282	283	286	285	286	284		285	284	289	288	291	291	295	297	294	293	288	295	300	295	303	297
4372	112	M	279	272	272	273	275	275	279	283	283	282		282	281	287	285	287	292	294	295	294	293	293	300	307	300	311	305
4372	575	F	186	181	182	179	183	181	186	184	184		186	190	190	190	192	188	194	192	199	194	196	192	199	199		201	202
4372	576	F	178	178	173	174	173	173	171	172	176		175	179	180	182	180	179	182	182	182	183	183	178	185	188	183	189	186
4372	577	F	181	176	175	177	178	174	175	173	178		176	180	183	185	183	180	184	183	185	182	182	178	180	183	178	182	183
4372	578	F	172	170	170	169	170	166	168	167	171		171	176	179	180	177	173	178	181	181	176	179	172	178	178	177	179	176
4372	579	F	177	175	176	176	178	179	173	170	179		179	179	184	185	188	184	187	188	191	189	192	184	192	196	193	193	196
4372	580	F	167	164	163	167	165	160	159	160	162		165	169	171	170	169	168	174	171	174	170	174	170	175	179	175	177	179
4372	581	F	191	188	187	187	186	183	187	185	188		189	192	195	196	195	191	198	192	201	199	199	194	200	204	201	205	203
4372	582	F	176	171	174	176	176	175	176	174	175		175	176	180	182	178	175	181	181	184	180	182	177	182	189	185	190	189
4372	583	F	187	186	182	183	180	182	178	179	178		183	186	189	189	187	187	195	192	194	194	194	189	196	196	195	202	199
4372	584	F	174	168	170	172	174	171	173	174	172		173	177	179	181	176	178	181	179	183	182	182	179	182	184	184	187	186
4372	585	F	188	186	188	184	182	181	183	182	182		186	188	190	193	193	188	195	196	196	190	194	192	191	194	192	195	195
4372	586	F	172	171	171	171	170	165	169	171	167		165	171	173	172	175	172	180	178	180	176	177	174	179	178	178	183	180
4372	587	F	175	174	176	175	175	173	172	169	171		174	174	178	179	181	175	182	180	182	181	183	177	188	189	185	187	189
4372	588	F	172	167	168	168	171	167	164	166	169		163	172	176	178	178	177	179	177	181	178	177	173	180	183	178	180	181
4372	589	F	169	169	168	169	169	169	164	166	167		170	172	175	177	175	176	180	177	183	180	178	173	180	184	181	184	178

PHASE III, PART 1 ----- BODY WEIGHT IN GRAMS ON STUDY DAY:

EXPT	ANI	SEX	-1	3	6	10	13	17	20	24	27	31	32	34	38	41	45	48	52	55	59	62	66	69	73	76	80	83	87
4372	590	F	180	179	176	172	173	172	169	173	174		175	180	183	183	184	179	186	182	186	185	185	183	190	189	188	194	191
4372	591	F	174	171	157		168	166	169	166	168		169	178	179	182	181	180	183	182	182	182	186	181	190	188	186	188	186
4372	592	F	173	169	168	167	169	165	166	166	167		167	174	174	176	176	172	176	177	179	176	177	76	183	181	177	183	181
4372	593	F	172	165	164	165	165	165	166	169	167		168	172	174	175	176	174	180	177	182	178	181	77	182	182	183	186	183
4372	594	F	175	167	166	166	168	163	165	165	170		168	173	175	177	174	172	181	180	181	180	183	178	182	186	181	185	181
4372	595	F	176	176	175	177	175	174	172	175	173		177	179	184	183	183	179	185	183	185	184	187	177	183	187	184	186	182
4372	596	F	180	176	176	177	178	175	172	179	176		178	181	182	186	185	183	188	184	189	183	189	184	187	189	188	188	188
4372	597	F	168	170	168	170	170	165	168	173	174		175	181	182	185	183	181	185	186	188	185	188	180	188	192	186	189	185
4372	598	F	183	182	184	181	183	176	178	174	177		181	183	186	184	186	183	187	185	190	190	189	183	190	191	188	188	187
4372	599	F	173	176	172	171	171	169	167	171	170		170	174	177	178	178	178	183	182	187	182	182	179	190	188	188	191	192
4372	600	F	162	163	160	162	161	155	160	163	161		163	167	168	166	170	169	173	170	175	172	173	169	174	175	174	176	176
4372	601	F	175	170	171	175	176	172	171	171	173		172	177	177	178	178	175	181	182	183	181	182	174	182	184	182	185	183
4372	602	F	173	169	172	171	170	169	171	169	171		172	175	178	178	178	176	181	179	182	179	179	172	182	183	180	180	180
4372	603	F	173	172	175	173	176	170	172	168	172		175	178	180	183	184	180	187	187	187	184	185	191	187	189	187	189	190
4372	604	F	174	172	167	168	158	163	168	172	172		168	173	175	178	175	177	180	180	184	180	179	175	181	181	176	179	178
4372	605	F	169	167	167	166	167	164	166	169	169		169	172	170	173	172	174	175	171	173	172	173	169	178	178	175	180	181
4372	606	F	182	183	180	180	179	182	179	179	181		182	186	186	186	190	186	192	188	192	189	189	183	189	190	187	190	191
4372	607	F	171	170	168	169	168	167	167	165	167		168	173	181	180	181	178	182	182	182	180	182	178	186	185	183	186	185
4372	608	F	174	174	171	172	173	173	170	175	173		176	178	177	180	179	175	183	183	186	182	184	180	184	187	183	189	188
4372	609	F	179	178	176	178	180	179	180	172	165		183	186	189	188	188	190	191	191	196	194	195	185	196	198	194	196	194
4372	610	F	172	167	166	164	166	166	162	166			168	173	167	172	175	174	178	177	179	179	176	174	179	180	175	180	175
4372	611	F	166	166	163	166	165	165	161	164	161		163	167	173	169	168	165	173	170	176	173	176	171	177	178	176	179	175
4372	612	F	172	180	167	164	166	161	161	164	163		166	172	172	172	170	170	176	176	179	176	177	169	175	180	176	178	
4373	113	M	297	291	288	286	287	291	289	293	289	289		291	293	296	294	297	298	292	293	298	293	292	296	300	295	306	297
4373	114	M	291	284	283	283	286	289	289	291	290	288		287	287	291	288	296	301	299	300	299	296	293	297	304	301	310	299
4373	115	M	289	283	281	284	286	286	287	290	290	291		289	295	299	294	300	303	304	303	308	304	301	308	311	306	320	311
4373	116	M	281	276	273	271	275	277	277	277	273	278		282	281	283	279	284	283	286	285	284	286	284	287	293	285	293	287
4373	117	M	279	268	273	272	275	276	276	277	274	274		272	273	280	274	281	282	287	288	286	288	284	289	296	288	296	291
4373	118	M	296	276	293	292	295	294	297	300	296	300		296	302	307	307	313	313	318	316	312	318	314	322	327	319	330	321
4373	119	M	294	287	282	281	282	284	285	287	284	281		283	282	288	283	291	293	293	291	291	291	291	295	299	291	300	292
4373	120	M	269	266	264	266	264	268	268	268	264	268		268	266	271	274	272	281	281	280	277	283	284	290	291	284	286	278
4373	121	M	277	272	267	268	268	268	272	271	271	270		271	272	278	273	277	280	280	279	282	281	277	282	287	283	292	282
4373	122	M	295	291	289	289	292	296	299	297	293	296		296	297	302	294	305	310	314	312	311	313	311	315	323	312	323	318
4373	123	M	269	269	261		268	270	271	272	271	265		265	269	268	270	272	282	282	286	283	288	282	289	294	285	296	288
4373	124	M	278	273	262		268	270	271	272	271	268		272	278	280	276	277	284	283	289	281	285	279	290	292	286	296	292
4373	125	M	284	281	278	280	280	283	278	284	286	284		284	286	292	287	294	297	293	292	298	296	291	297	301	294	305	293
4373	126	M	276	276	272	273	274	274	271	279	277	274		275	280	284	282	283	286	290	287	285	289	281	288	291	286	296	288
4373	127	M	272	275	265	267	264	264	266	265	261	265		272	273	277	276	279	282	282	283	284	284	284	290	291	284	294	286
4373	128	M	282	293	275	277	274	271	275	278	277	278		281	283	288	284	288	290	294	297	293	296	296	296	297	298	307	299
4373	129	M	286	276	276	275	279	278	273	279	278	281		284	281	288	282	283	288	292	290	294	293	289	299	300	294	264	258
4373	130	M	277	273	269	270	274	276	273	276	276	277		279	279	282	277	280	282	287	286	282	285	279	287	289	283	289	287

PHASE III, PART 1 ----- BODY WEIGHT IN GRAMS ON STUDY DAY:

EXPT	ANI	SEX	-1	3	6	10	13	17	20	24	27	31	32	34	38	41	45	48	52	55	59	62	66	69	73	76	80	83	87
4373	131	M	268	263	260	260	260	262	261	264	261	265		266	267	270	268	268	275	274	277	277	275	274	280	284	281	282	285
4373	132	M	276	264	260	258	258	262	259	262	260	264		260	270	272	270	269	275	275	277	274	279	272	281	284	282	291	278
4373	133	M	271	269	268	269	268	268	265	266	263	268		270		274	268	276	277	282	283	280	283	281	284	288	284	291	288
4373	134	M	274	265	265	268	269	273	271	281	276	277		282		291	288	295	296	300	300	303	303	298	306	309	300	311	300
4373	135	M	262	260	257	251	256	257	259	264	260	263		261		271	268	276	275	276	279	280	283	278	284	284	282	287	288
4373	136	M	289	282	278	276	280	279	277	279	278	278		275		283	278	283	285	288	288	290	289	282	290	291	283	292	288
4373	137	M	292	288	285	285	285	285	281	283	279	282		283	282	290	293	296	296	299	303	302	303	299	307	309	306	313	303
4373	138	M	279	268	266	267	267	269	269	273	269	275		274		282	280	283	288	281	289	290	285	285	291	293	287	295	290
4373	139	M	282	275	272	276	278	279	279	282	281	285		287		295	289	292	294	297	299	293	295	291	302	307	298	307	302
4373	140	M	268	263	263	263	267	270	270	272	268	272		268		270	272	277	278	279	279	280	281	273	281	285	280	293	285
4373	141	M	288	277	275	274	279	279	282	283	283	283		288	285	293	289	295	295	298	301	298	299	300	300	302	299	312	300
4373	142	M	273	266	263	265	269	272	275	279	278	281		284	287	287	285	287	292	289	295	296	296	300	301	305	300	310	299
4373	143	M	281	282	275	275	280	278	280	284	284	287		281	287	294	287	294	292	296	294	289	292	290	299	305	292	300	294
4373	144	M	278	275	274	276	277	283	284	283	283	287		284	291	293	292	295	296	293	296	296	296	293	298	297	295	303	296
4373	145	M	288	283	283	280	282	279	283	285	286	288		289	283	287	281	287	290	293	292	291	294	289	295	299	292	303	294
4373	146	M	270	265	260	262	264	260	265	269	272	275		276	275	280	274	277	277	279	277	279	278	280	281	283	278	286	273
4373	147	M	284	281	278	280	282	280	281	282	279	283		282	282	283	281	280	288	289	286	282	286	284	285	288	281	288	282
4373	148	M	287	284	277	279	284	284	287	290	288	288		288	289	293	288	289	298	293	296	292	290	285	291	293	289	295	295
4373	149	M	288	283	281	280	285	288	287	290	290	290		294	294	295	295	298	306	301	296	299	303	299	305	306	303	304	297
4373	150	M	278	274	269	270	273	274	274	276	282	284		287	286	288	284	285	295	292	297	297	295	290	299	301	295	305	299
4373	613	F	183	180	180	180	180	173	174	174	177		178	184	185	187	186	180	186	186	189	187	189	185	188	190	185	191	189
4373	614	F	176	175	176	174	175	174	174	173	176		176	183	187	189	188	186	190	193	193	190	189	183	188	192	186	190	181
4373	615	F	177	173	171	169		163	167	167	171		173	175	174	176	176	176	178	181	182	181	179	173	181	182	181	183	182
4373	616	F	180	177	176	176	174	171	172	173	174		177	176	176	177	180	177	179	183	184	182	180	180	182	186	184	184	181
4373	617	F	175	174	172	172	171	164	165	164	169		169	173	177	178	180	179	180	182	182	183	182	178	183	183	183	186	181
4373	618	F	167	166	163	159	159	155	155	154	156		158	164	167	169	166	169	171	171	170	170	168	165	171	172	171	173	171
4373	619	F	164	160	160	157	159	158	158	164	161		159	165	164	167	166	164	170	166	171	169	169	164	170	175	171	173	172
4373	620	F	185	181	178	177	176	174	172	173	173		172	179	179	184	181	183	187	185	183	186	185	180	186	190	183	186	183
4373	621	F	185	181	168	174	175	175	178	178	176		179	182	183	186	185	186	189	186	191	186	188	183	190	192	187	189	184
4373	622	F	174	171	176	168	168	168	169	172	169		173	177	178	179	182	180	187	184	191	186	190	184	188	192	189	191	188
4373	623	F	182	184	180	179	181	180	184	185	186		185	187	189	188	192	188	192	192	194	194	195	189	197	197	195	196	194
4373	624	F	169	166	163		158	163	168	167	167		168	172	171	177	176	173	176	178	177	177	179	175	186	180	176	180	175
4373	625	F	183	178	176	173	178	173	175	175	177		178	181	183	187	186	181	186	185	186	183	187	184	187	187	185	189	186
4373	626	F	184	182	165		181	178	181	183	181		179	184	187	186	184	182	184	184	189	185	189	184	176	189	187	190	186
4373	627	F	175	175	173	167	168	169	172	168	170		169	171	175	177	177	176	176	178	180	179	178	175	178	180	177	179	178
4373	628	F	171	169	166	164	165	164	162	164	163		166	167	173	177	174	175	175	175	176	173	174	175	183	179	177	177	174
4373	629	F	176	168	170	166	172	172	169	174	171		173	176	176	178	175	175	177	179	180	176	178	180	185	180	182	185	182
4373	630	F	171	171	172	171	172	174	173	173	173		174	174	179	180	182	180	183	183	187	187	185	181	174	186	183	189	187
4373	631	F	171	167	165	165	168	165	166	165	163		168	173	173	173	172	171	173	171	172	173	172	167	176	176	172	175	173
4373	632	F	171	166	165	163	167	152	156	166	167		169	171	174	176	177	177	179	176	178	177	175	170	176	180	177	182	178

PHASE III, PART 1 ----- BODY WEIGHT IN GRAMS ON STUDY DAY:

EXPT	ANI	SEX	-1	3	6	10	13	17	20	24	27	31	32	34	38	41	45	48	52	55	59	62	66	69	73	76	80	83	87
4373	633	F	171	168	163	164	162	161	164	155	153		163	168	169	173	172	174	180	178	179	175	175	169		178	176	180	176
4373	634	F	182	184	182	181	180	184	179	174	177		181	184	183	182	182	183	188	186	186	188	187	186	181	190	188	190	186
4373	635	F	175	171	170	167	169	167	167	170	169		172	175	178	177	179	176	179	180	180	178	178	173		180	179	180	178
4373	636	F	185	182	182	182	183	183	181	181	182		185	188	189	192	194	187	195	195	199	193	196	193		196	195	197	193
4373	637	F	167	163	161	150	143	150	152	155	154		157	164	162	167	163	163	164	169	169	168	170	167	165	169	166	170	166
4373	638	F	164	162	160	158	158	157	158	160	158		161	164	164	165	165	165	163	167	171	172	172	178		151	162	169	171
4373	639	F	181	177	174	175	179	178	177	173	175		177	182	180	181	182	181	185	184	186	181	186	185	182	188	189	190	190
4373	640	F	176	168	164	167	171	167	164	171	172		175	182	184	184	180	179	182	179	185	180	185	183	183	185	179	185	184
4373	641	F	172	174	172	173	174	171	168	171	165		172	174	176	180	179	178	182	181	182	179	180	182		185	181	183	179
4373	642	F	172	169	165	166	166	163	158	162	162		162	168	166	167	166	167	169	167	170	170	169	167	175	169	167	170	170
4373	643	F	174	170	170	166	163	161	160	162	146		151	161	169	172	170	171	176	178	176	175	174	171	186	176	175	180	172
4373	644	F	175	175	172	171	174	171	173	172	174		172	178	180	183	181	178	183	182	187	183	187	179	191	187	187	190	189
4373	645	F	176	172	171	172	174	173	166	174	173		179	182	184	187	184	182	189	186	189	185	189	185	183	193	190	193	192
4373	646	F	173	169	169	169	168	168	170	166	166		171	172	175	177	178	175	182	181	183	182	180	176	182	184	182	184	179
4373	647	F	181	179	176	171	172	169	167	173	169		172	177	179	181	176	176	178	183	180	181	180	175	175	187	183	188	183
4373	648	F	165	163	147	156	159	158	155	161	162		165	165	169	172	171	171	174	177	176	174	173	167	175	178	172	176	172
4373	649	F	180	180	175	172	173	172	171	167	167		170	171	170	175	176	171	178	178	179	176	179	179	181	184	180	183	181
4373	650	F	167	169	165	163	163	163	160	165	163		166	166	173	168	172	169	177	172	175	172	172	172	176	180	177	180	174

PHASE III, PART 2 ---- BODY WEIGHT IN GRAMS ON STUDY DAY:

EXPT	ANI	SEX	-2	2	5	9	12	16	19	23	26	30	33	37	40	44	47	51	54	58	61	65	68	72	75	79	82	86	89
4442	101	M	294	293	285	284	291	285	294	302	302	305	301	303	298	303		302	302	303	302	302	296	299	299	303	303	307	302
4442	102	M	299	299	296	293	300	301	306	307	310	315	314	315	321	316	304	311	314	309	311	317	315	320	316	324	328	328	324
4442	103	M	299	293	292	290	293	294	304	304		293	296	303	307	302	293	304	307	311	303	303	304	309	306	314	309	315	311
4442	104	M	292	295	295	292	300	290	299	291	304	306	306	305	308	316		305	304	305	310	312	315	318	318	325	331	332	321
4442	105	M	289	289	284	287	293	286	292	296	297	297	300	295	304	294	287	302	301	304	305	308	309	310	313	315	316	318	
4442	106	M	300	296	296	300	303	298	300	308	310	318	314	315	313		312	318	323	322	327	323	322	329	324	327	332	338	335
4442	107	M	299	304	304	301	306	301	308	313	317	316	317	306	305	315		318	322	321	323	323	327	336	332	342	339	336	332
4442	108	M	305	302	301	304	310	311	318	319	325	327	328	333	335	334		330	331	332	333	331	328	336	332	342	338	343	340
4442	109	M	319	317	315	305	315	309	315	312	314	315	318	319	322	319	314	318	322	322	325	330	328	330	328	336	339	336	337
4442	110	M	305	308	300	297	308	305	315	310	312	310	313	311	317	313	310	315	314	311	311	305	305	302	306	307	301	301	303
4442	111	M	296	291	291	289	297	292	298	296	300	298	296	303	302	303	300	306	307	301	305	301	303	306	303	305	312	299	310
4442	112	M	300	296	295	297	302	301	308	307	311	311	305	312	304	303	304	309	312	307	312	313	310	319	313	324	321	329	341
4442	113	M	300	298	294	291	299	296	299	302	300	305	296	304	303	297	300	306	306	304	307	307	305	309	310	308	312	308	320
4442	114	M	295	295	287	286	289	290	299	299	299	304	302	307	311	308	303	310	311	313	309	315	312	319	315	320	322	324	320
4442	115	M	305	301	298	296	303	301	307	308	309	307	303	310	308	309	310	312	319	314	314	314	318	325	326	328	332	327	327
4442	116	M	298	299	294	290	293	293	302	304	303	305	302	305	303	305	300	306	310	312	314	323	317	325	325	328	328	329	323
4442	117	M	301	301	296	291	299	296	302	306	309	312	307	312	311	305	301	308	310	312	311	314	311	317	315	321	322	324	325
4442	118	M	302	298	294	286	293	286		283	288	295	298	297	300	300	292	300	300	300	304	300	303	305	304	307	307	309	302
4442	119	M	308	300	295	294	300	300	304	303	306	308	304	307	305	306	300	307	306	310	304	308	306	314	314	316	316	316	319
4442	120	M	305	282	281	291	300	295	301	306	308	318	309	305	312	313	304	314	315	316	317	315	316	316	318	320	321	324	321
4442	121	M	302	301	299	295	300	299	302	304	307	316	312	310	316	313	311	319	321	319	322	325	325	327	328	328	320	329	326
4442	122	M	303	303	301	302	307	308	310	311	312	317	317	317	318	317	318	320	323	321	321	332	327	334	336	338	336	333	329
4442	123	M	297	298	294	289	295	291	298	297	300		300	304	309	310	298	308	307	311	309	305	304	313	312	316	315	317	316
4442	124	M	302	297	292	293	296	296	303	306	305	309	306	310	315	314	308	317	320	314	320	321	320	329	325	328	332	338	
4442	125	M	311	305	302	306	309	308	311	318	317	316	313	314	316	320	316	323	322	326	325	323	323	325	325	328	328	329	328
4442	126	M	303	305	304	302	301	303	306	309	314	321	312	316	318	317	315	322	324	327	323	319	324	331	331	333	333	332	329
4442	127	M	307	304	298	299	303	304	308	312	315	317	316	319	319	316	313	324	325	333	324	329	327	336	334	334	335	335	333
4442	128	M	315	305	299	301	302	300	307	305	311	313	309	317	316	313	309	318	316	316	312	320	315	319	320	322	323	324	318
4442	129	M	308	311	297	298	302	300	307	312	314	310		296	298	303	301	308	314	312	305	312	311	314	311	318	317	323	316
4442	130	M	313	305	309	310	316	313	320	321	326	324	323	326	330	328	327	327	332	334	327	333	327	334	337	336	342	339	335
4442	131	M	301	301	292	289	294	288	291	294	297	300	297	299	304	303	303	311	310	311	307	311	312	315	310	311	314	309	312
4442	132	M	321	322	316	312	320	314	323	321	319	314	316	317	321	321	318	324	326	323	323	319	320	325	326	331	339	332	331
4442	133	M	301	298	297	302	303	297	302	305	308	310	309	305	312	313	311	312	314	318	319	318	316	322	326	330	334	325	327
4442	134	M	315	311	306	303	311	310	316	314	312	317	317	315	320	314	310	315	314	323	317	319	320	322	325	330	335	327	332
4442	135	M	311	305	301	308	305	305	308	308	312	316	314	315	319	318	315	319	317	316	316	320	319	319	325	327	331	328	329
4442	136	M	313	309	304	302	308	306	309	312	314	316	316	318	321	321	315	322	323	325	323	325	325	332	331	330	335	331	329
4442	137	M	311	308	305	300	311	309	307	309	317	318	318	316	317	314	315	321	325	325	326	326	329	334	334	331	340	338	337
4442	138	M	295	297	292	292	296	294	297	296	299	304	304	310	310	308	310	316	318	319	324	319	320	324	325	324	326	325	328
4442	501	F	172	170	165	170	172	171	174	179	175	179	177	176	176	175	172	172	171	175	173	177	175	181	179	181	183	182	177
4442	502	F	180	180	175	175	180	178	178	178	181	186	183	183	185	186	181	186	186	189	188	187	186	190	187	193	194	191	190

PHASE III, PART 2 ---- BODY WEIGHT IN GRAMS ON STUDY DAY:

EXPT	ANI	SEX	-2	2	5	9	12	16	19	23	26	30	33	37	40	44	47	51	54	58	61	65	68	72	75	79	82	86	89
4442	503	F	190	191	188	192	190	188	191	194	194	200	193	195	195	197	195	194	196	196	194	194	195	200	195	205	205	202	209
4442	504	F	171	172	168	173	172	173	173	175	176	179	176	179	180	181	179	181	182	185	180	186	183	185	185	189	189	189	187
4442	505	F	195	195	185	187	187	185	191	195	194	198	193	193	196	197	194	194	194	200	197	199	196	196	198	200	204	203	195
4442	506	F	183	181	175	177	179	175	175	178	176	179	177	182	182	180	178	181	176	184	181	185	179	184	183	187	183	187	182
4442	507	F	175	177	171	183	175	176	177	178	176	183	182	182	183	180	175	184	182	182	181	183	179	189	184	186		185	183
4442	508	F	182	179	177	180	182	181	181	187	184	190	179	185	187	181	178	185	184	188	185	186	181	191	181	190	188	188	183
4442	509	F	178	180	176	176	177	178		179	181	182	181	185	181	183	180	184	183	188	183	186	184	192	186	197	194	192	193
4442	510	F	181	179	177	180	181	180	168	181	179	186	183	187	184	186	182	188	190	190	187	195	187	195	188	194	189	193	188
4442	511	F	170	170	168	169	171	173	174	178	176	180	175	180	181	184	180	182	186	189	182	187	181	189	185	190	189	190	185
4442	512	F	174	172	173	173	175	177	175	174	173	177	175	176	175	175	171	177	176	178	178	174	173	174	174	179	179	174	177
4442	513	F	190	189	184	185	190	189	191	195	193	193	191	192	197	191	192	193	194	197	194	194	190	201	198	195	200	198	192
4442	514	F	169	172	169	168	173	175	173	175	177	177	176	174	178	177	178	179	181	179	178	179	180	184	182	181	184	179	192
4442	515	F	183	184	180	181	183	183	187	185	185	185	185	188	187	187	187	192	192	197	192	191	188	194	188	194	194	197	192
4442	516	F	179	180	178	180	182	179	184	185	184	190	186	187	187	184	185	187	190	190	187	186	188	188	186	189	191	189	190
4442	517	F	185	184	185	186	186	188	188	188	188	192	189	192	192	197	189	190	195	192	191	187	187	194	194	194	202	198	194
4442	518	F	188	188	187	189	190	187	195	193	197	200	198	200	195	196	192	196	201	205	197	200	197	200	201	207	200	203	196
4442	519	F	182	183	182	184	182	177	183	185	186	195	187	190	189	186	186	190	189	188	172	177	179	191	192	196	197	198	196
4442	520	F	175	175	173	176	173	173	173	176	178	179	178	178	180	181	178	180	177	193	182	181	179	185	184	185	183	185	183
4442	521	F	185	184	181	183	187	186	185	190	188	189	181	184	184	183	181	186	193	188	188	185	186	188	191	190	188	191	188
4442	522	F	182	181	179	179	176	179	180	184	184	187	183	186	186	187	184	188	188	192	188	187	188	190	194	196	195	189	192
4442	523	F	183	184	183	186	189	183	189	190	189	190	187	188	188	187	186	191	194	192	192	191	189	194	195	196	191	196	191
4442	524	F	175	176	177	177	175	174	174	178	182	184	177	180	181	182	179	182	185	185	183	183	182	185	183	191	188	188	183
4442	525	F	190	192	186	187	190	188	186	190	191	192	190	194	193	191	188	191	193	195	194	192	190	195	196	200	199	199	190
4442	526	F	177	179	176	179	179	178	178	184	181	183	179	179	180	179	179	182	187	186	181	183	181	183	184	186	187	187	186
4442	527	F	184	185	182	184	186	186	182	190	186	188	186	187	187	189	185	188	192	188	187	189	189	191	190	192	195	200	194
4442	528	F	180	179	176	174	177	173	176	178	179	178	176	176	178	180	179	181	180	179	178	179	180	185	186	189	189	185	198
4442	529	F	174	177	176	178	179	177	178	182	182	190	181	182	182	183	181	183	188	186	185	184	182	186	188	195	187	190	186
4442	530	F	172	174	174	174	173	174	176	181	180	180	179	178	182	182	187	184	183	185	182	181	181	184	188	189	189	185	179
4442	531	F	185	188	187	192	191	189	188	194	192	194	191	191	188	189	183	191	196	192	189	191	186	197	191	196	193	198	192
4442	532	F	185	182	183	185	186	185	185	186	188	189	189	186	181	182	181	183	187	184	183	183	183	185	192	188	187	186	185
4442	533	F	177	179	176	179	181	181	180	187	183	186	181	184	195	183	182	185	187	183	184	184	178	183	186	188	191	191	189
4442	534	F	185	183	183	188	189	186	187	193	188	193	191	191	188	190	188	190	192	191	190	189	185	191	192	192	194	193	187
4442	535	F	184	184	178	181	182	182	183	183	189	188	186	186	186	187	187	189	192	192	190	189	187	192	191	191	192	191	191
4442	536	F	181	182	175	178	180	179	179	183	183	187	183	185	184	183	180	182	190	187	189	187	184	189	193	192	192	194	191
4442	537	F	179	180	178	179	183	184	183	189	190	193	192	197	192	193	191	194	202	201	196	198	194	197	201	200	202	196	191
4442	538	F	184	183	178	179	183	179	180	187	185	186	184	183	185	184	183	185	187	185	185	186	181	184	186	188	186	182	183
4443	139	M	299	297	292	289	299	298	303	303	308	316	310	314	313	315	310	319	318	319	314	319	314	320	323	331	325	324	329
4443	140	M	303	304	296	292	302	296	303	305	306	311	308	311	311	309	311	314	313	316	319	319	312	319	319	323	320	320	313
4443	141	M	302	303	295	295	299	295	300	310	310	312	310	309	315	320	316	320	318	321	321	325	327	332	322	326	330	336	330
4443	142	M	316	316	311	306	311	307	316	319	317	323	317	321	322	325	316	324	326	329	321	326	320	327	324	328	333	336	330

PHASE III, PART 2 ---- BODY WEIGHT IN GRAMS ON STUDY DAY:

EXPT	ANI	SEX	-2	2	5	9	12	16	19	23	26	30	33	37	40	44	47	51	54	58	61	65	68	72	75	79	82	86	89
4443	143	M	301	300	296	294	298	296	301	298	302	304	303	302	305	307	307	309	313	312	313	314	315	318	317	319	318	323	317
4443	144	M	304	302	297	301	303	304	307	312	309	279	291	[illegible]	304	304	304	310	310	312	309	314	310	322	315	322	322	322	317
4443	145	M	294	298	288	294	293	292	299	301	302	303	301	304	306	306	302	308	313	315		314	313	317	321	324	324	324	318
4443	146	M	304	302	300	304	306	306	310	318	320	320	319	324	324	329	326	331	330	330	323	337	333	339	331	337	340	340	333
4443	147	M	314	308	296	304	306	296	311	315	317	318	317	[illegible]	319	319	310	316	320	323	320	323	318	328	326	332	320	331	323
4443	148	M	299	300	296	296	300	297	309	306	309	311	308	313	316	318	315	316	322	320		324	327	325	333	328	323	327	326
4443	149	M	299	296	289	288	289	280	290	295	298	299	299	296	300	297	295	304	303	302		305	304	310	327	308	312	315	305
4443	150	M	308	305	302	307	312	307	314	317	316	317	313	315	315	314	311	318	319	319	319	315	318	318	329	322	322	324	319
4443	151	M	312	310	305	301	307	303	306	310	313	315	314	314	316	316	312	318	321	334	327	320	317	326	327	326	328	325	324
4443	152	M	308	312	308	306	309	309	312	314	317	322	319	322	324	319	319	331	329	320	326	332	327	338	333	346	333	340	332
4443	153	M	303	304	299	307	308	302	312	317	316	318	314	313	317	316	316	318	322	321	321	326	322	325	331	331	334	334	332
4443	154	M	307	303	294	299	303	302	305	311	310	310	305	305	312	311	312	312	316	291	300	304	309	311	315	320	322	324	316
4443	155	M	299	301	294	288	296	293	297	298	303	301	302	301	306	302	300	303	308	308	309	308	309	312	314	321	318	320	319
4443	156	M	315	313	305	304	310	310	313	316	316	323	321	313	319	317	332	320	326	323	326	327		332	336	335	339	337	337
4443	157	M	325	326	319	319	326	323	327	330	332	334	328	331	331	335	331	338	339	336	334	335	335	342	342	344	348	347	346
4443	158	M	300	299	295	295	300	297	305	309	310	310	307	306	307	304	305	311	312	312	309	314	305	315	319	320	319	324	316
4443	159	M	308	302	298	287	258	279	295	299	302	308	307	303	312	305	306	307	315	312	315	311	313	316	321	318	321	321	316
4443	160	M	293	292	299	283	287	277	286	285	289	289	286	288	290	286	286	290	295	300	297	293	294	297	299	304	302	303	300
4443	539	F	174	179	180	180	184	179	166	187	168	173	171	173	173	178	176	179	178	179	177	180	178	185	181	182	181	181	175
4443	540	F	176	170	165	163	164	165	186	168	187	190	187	187	187	189	184	187	188	186	185	180	181	188	183	188	187	192	184
4443	541	F	168	169	164	167	169	169	169	172	169	173	170	171	172	173	170	175	176	178	176	177	179	179	178	181	181	181	177
4443	542	F	186	182	182	185	188	190	186	191	190	195	194	192	195	190	189	195	196	178	197	200	200	198	200	200	202	199	194
4443	543	F	185	177	178	184	182	185	183	183	185	186	185	184	186	187	186	188	190	188	187	186	189	190	190	193	190	185	189
4443	544	F	181	180	173	177	179	178	178	182	184	187	182	185	187	187	184	190	190	190	188	184	195	195	192	193	193	192	192
4443	545	F	176	181	180	181	184	183	187	200	188	193	194	192	196	195	194	198	196	200	196	198	194	198	199	200	201	201	198
4443	546	F	171	172	172	176	179	177	179	180	182	186	183	183	181	181	181	184	186	188	189	186	187	189		196	190	188	184
4443	547	F	181	176	177	175	177	177	176	180	181	182	182	179	182	185	184	187	190	187	185	183	184	182		182	185	184	181
4443	548	F	183	184	185	184	188	188	188	190	190	195	192	193	192	193	191	194	194	197	194	197	193	198	198	202	198	200	192
4443	549	F	179	178	175	177	180	180	181	183	184	187	185	182	187	184	184	187	188	191	187	182	187	192	190	195	195	189	192
4443	550	F	176	175	174	173	177	175	179	181	178	181	178	186	181	183	183	186	186	185	182	186	187	190	187	191	192	191	184
4443	551	F	194	191	191	190	191	192	193	196	195	198	192	196	195	197	194	200		202	194	198	195	187	192	200	198	205	199
4443	552	F	180	176	177	178	179	180	180	183	181	187	184	186	185	186	183	185	190	187	185	189	186	198	190	191	189	190	187
4443	553	F	192	191	188	186	189	190	185	190	192	195	191	194	193	192	189	193	195	196	193	194	189	197	195	196	198	200	190
4443	554	F	186	188	183	186	187	189	186	190	189	195	190	195	191	191	189	191	192	195	192	192	191	188	192	196	196	199	188
4443	555	F	180	181	177	176	179	182	176	183	184	185	181	182	185	184	182	186	185	185	184	184	182	177	187	190	191	189	189
4443	556	F	175	177	172	171	172	176	173	176	176	177	174	176	176	174	171	177	177	179	176	179	173	177	176	180	177	182	176
4443	557	F	185	187	185	184	183	185	184	190	188	193	188	193	193	191	189	194	191	195	191	190	185	195	192	198	197	199	194
4443	558	F	175	175	173	171	176	176	177	181	179	182	182	181	181	181	179	184	186	190	185	191	183	192	186	193	186	193	190
4443	559	F	177	176	179	178	179	183	179	181	181	187	184	185	184	183	180	186	183	185	182	189	179	191	184	189	194	188	181
4443	560	F	178	181	174	175	181	177	178	179	180	180	179	180	177	180	177	179	180	180	178	177	177	180	180	182	180	178	192

PHASE III, PART 2 ---- BODY WEIGHT IN GRAMS ON STUDY DAY:

EXPT	ANI	SEX	-2	2	5	9	12	16	19	23	26	30	33	37	40	44	47	51	54	58	61	65	68	72	75	79	82	86	89
4444	161	M	295	295	291	281	292	290	295	299	300	300	296	296	295	293	290	295	300	297	294	300	303	306	301	304	306	308	305
4444	162	M	287	287	281	279	285	291	291	293	298	301	296	297	295	291	288	293	297	297	297	299	295	305	308	308	311	305	301
4444	163	M	299	291	290	290	297	292	300	305	305	308	305	303	305	298	299	307	311	309	313	314	311	320	319	321	319	326	321
4444	164	M	307	305	301	298	302	300	306	310	308	310	311	315	317	311	308	313	323	322	324	320	325	324	320	331	332	332	330
4444	165	M	302	295	293	293	299	294	298	305	304	309	307	310	314	307	302	304	310	312	312	308	311	316	315	324	322	322	323
4444	166	M	292	294	285	285	290	285	292	296	296	300	294	297	300	297	293	296	296	298	298	305	305	309	307	310	312	314	310
4444	167	M	308	302	303	301	304	297	300	305	306	305	306	304	304	301	299	301	305	303	303	307	305	309	313	313	315	313	316
4444	168	M	305	303	301	299	303	287	297		290	297	296	299	300	298	295	298	303	305	306	308	304	304	310	311	313	312	313
4444	169	M	304	304	302	304	307	299	304	306	308	311	307	307	313	307	311	311	311	313	309	306	305	314	309	315	309	307	308
4444	170	M	309	308	303	304	304	299	303	310	310	310	307	304	308	307	308	315	315	318	321	316	319	319	318	326	324	324	323
4444	171	M	304	304	298	293	297	297	304	303	309	306	310	307	311	306	304	306	315	315	310	311	308	317	315	319	316	318	314
4444	172	M	316	319	314	314	311	309	300	316	320	326	323	321	329	326	329	331	334	337	330	331	336	333	338	339	340	341	336
4444	173	M	298	297	291	289	291	291	304	305	307	309	308	308	304	307	305	311	311	313	315	312	310	317	313	319	323	319	318
4444	174	M	297	300	294	299	301	294	308	306	310	311	309	309	304	304	301	307	310	304	303	305	300	307	309	311	314	316	311
4444	175	M	308	309	305	304	307	312	310	309	315	318	316	317	320	318	317	320	327	322	326	325	325	331	333	338	338	337	336
4444	176	M	302	303	294	298	301	299	306	293	291	305	309	313	317	314	315	319	319	318	320	324	319	330	326	327	332	330	330
4444	177	M	305	303	294	293	299	300	306	308	314	313	313	315	321	319	317	320	325	325	331	330	324	328	329	325	335	335	332
4444	178	M	287	288	284	282	283	287	290	292	294	294	296	301	303	308	297	307	309	313	310	315	312	316	316	317	316	314	316
4444	179	M	302	302	297	299	303	300	309	310	314	314	312	314	313	316	316	313	322	320	321	324	321	333	331	337	338	333	335
4444	180	M	310	309	302	299	304	301	303	307	312	308	307	309	313	310	308	310	317	318	320	314	311	316	314	325	311	321	335
4444	181	M	303	299	298	295	300	298	304	304	307	308	306	301	304	302	301	307	309	306	307	306	301	310	312	318	317	319	313
4444	182	M	305	301	295	293	299	296	299	302	306	308	308	310	309	310	308	312	312	314	315	312	309	315	311	316	318	316	312
4444	183	M	295	291	288	289	291	291	295	298	302	305	300	301	304	306	301	308	306	310	306	308	308	315	316	322	321	324	319
4444	184	M	290	289	287	286	291	307	298	300	301	304	302	304	308	304	305	308	308	313	308	310	307	318	317	321	324	325	317
4444	185	M	303	303	295	295	302	293	299	303	306		295	299	304	307	304	308	318	308	317	316	309	316	320	322	330	321	325
4444	186	M	311	308	308	305	310	311	297	317	320		320	321	323	319	317	318	323	319	322	320	316	325	324	328	327	327	325
4444	187	M	287	284	284	289	291	289	306	303	305	310	303	306	310	306	306	307	309	306	306	310	310	318	315	324	329	332	328
4444	188	M	306	304	299	301	302	299	305	308	311	310	310	306	306	300	299	304	310	309	310	310	310	313	314	318	318	317	312
4444	189	M	304	305	303	299	307	292	293	300	310	299	311	301	300	300	300	304	309	306	308	312	317		326	324	332	328	324
4444	190	M	293	288	288	287	290	302	310	310	299	310	299	306	311	308	309	307	312	317	314	316	305		310	314	316	317	309
4444	191	M	300	297	293	286	292	289	297	296	298	303	300	298	304	303	303	310	310	312	311	313	309	305	314	324	320	323	319
4444	192	M	299	298	299	297	299	293	300	304	303	304	304	303	309	306	305	312	314	322	319	322		312	311	323	323	328	322
4444	193	M	298	298	292	291	295	293	293	297	301	304	303	306	306	306	305	306	309	306	305	307	306	310	302	310	308	303	308
4444	194	M	300	300	295	296	303	299	305	309	311	314	314	318	319	317	317	318	327	323	332	332	330	337	334	335	348	338	338
4444	195	M	302	300	300	301	304	300	303	313	306	312	313	316	315	319	315	317	319	325	319	315	311	319	319	326	324	321	324
4444	196	M	300	298	294	295	301	301	306	308	315	321	314	317	319	323	314	323	323	318	324	327	320	327	327	320	331	334	329
4444	197	M	309	309	303	304	303	296	308	310	309		308	305	309	302	307	311	315	314	315	317	312	321	313	323	323	324	317
4444	198	M	321	313	316	316	320	307	321	323	322		322	319	321	318	317	324	331	328	335	332	335	333	331	337	339	331	330
4444	561	F	174	171	171	176	156	166	168	178	177	181	181	183	182	181	182	184	185	188	184	186	185	189	189	197	191	195	187
4444	562	F	166	171	173	176	177	179	183	188	187	188	184	188	185	183	182	188	187	188	185	188	181	187	187	192	191	195	181

PHASE III, PART 2 ---- BODY WEIGHT IN GRAMS ON STUDY DAY:

EXPT	ANI	SEX	-2	2	5	9	12	16	19	23	26	30	33	37	40	44	47	51	54	58	61	65	68	72	75	79	82	86	89
4444	563	F	172	172	170	168	172	171	174	175	173	180	177	174	177	180	176	180	179	181	178	183	181	181	185	191	187	189	184
4444	564	F	181	183	180	181	186	187	185	189	188	193	190	191	194	192	188	193	198	195	193	194	175	196	198	198	199	205	193
4444	565	F	184	181	178	178	180	181	178	182	182	185	176	181	181	181	179	185	184	192	184	186	180	185	183	187	184	196	199
4444	566	F	183	183	181	186	183	186	187	188	190	191	188	178	170	184	183	191	194	195	183	197	192	198	197	199	200	200	194
4444	567	F	179	179	182	183	183	184	182	187	182	190	184	189	186	188	185	189	190	192	189	193	193	196	194	197	193	199	
4444	568	F	181	181	181	184	186	184	186	188	189	192	185	188	187	186	184	187	188	191	184	187	185	188	187	193	188	193	187
4444	569	F	176	178	174	176	177	176	179	181	183	186	183	188	185	185	183	189	191	192	187	190	190	193	189	196	196	196	191
4444	570	F	180	179	175	177	178	176	176	179	178	179	175	177	174	178	177	181	184	183	183	181	179	186	183	187	182	187	182
4444	571	F	185	182	182	184	183	182	180	181	183	182	180	183	183	183	180	184	186	187	189	184	180	191	189	190	188	190	186
4444	572	F	182	178	178	179	181	180	183	184	185	187	185	191	185	189	184	186	186	190	188	186	183	188	186	188	185	184	183
4444	573	F	172	171	169	167	173	173	173	176	175	179	174	178	177	180	176	180	181	182	176	180	177	181	177	183	180	180	179
4444	574	F	173	176	172	176	178	176	177	177	180	184	181	185	184	185	182	189	185	189	187	183	179	190	186	189	189	190	188
4444	575	F	185	185	181	179	182	180	178	182	178	182	175	181	183	181	178	183	184	185	183	182	175	187	180	185	188	186	179
4444	576	F	183	182	180	180	182	183	181	177	177	179	179	178	177	178	177	185	184	184	185	184	178	189	181	188	185	188	184
4444	577	F	180	177	174	174	172	173	175	179	180	184	182	185	186	188	181	183	186	187		185	184	190	186	190	192	190	184
4444	578	F	178	176	173	171	73	174	174	175	176	178	172	176	176	176	175	176	181	196	176	177	175	182	179	183	184	177	176
4444	579	F	191	193	190	195	199	195	190	196	194	199	197	201	196	196	196	198	198	196	198	197	196	201	198	200	200	197	195
4444	580	F	187	184	180	185	186	186	185	179	185	191	183	190	192	191	189	192	193	196	194	195	193	197	191	193	195	186	183
4444	581	F	177	175	172	176	179	174	176	180	175	180	177	180	186	180	179	179	184	186	181	184	180	187	181	183	191	187	184
4444	582	F	184	186	181	185	189	184	186	188	184	189	184	185	189	186	186	189	193	192	189	190	188	191	189	193	188	196	189
4444	583	F	177	179	178	180	181	182	180	177	188	190	186	187	183	176	186	189	184	191	188	188	187	195	188	195	191	197	193
4444	584	F	175	175	174	179	177	177	175	178	179	180	177	179	177	181	178	180	188	185	187	187	184	189	187	189	189	190	183
4444	585	F	177	174	175	177	180	177	179	176	179	182	176	180	180	185	179	180	178	186	183	184	182	187	183	187	191	185	183
4444	586	F	187	184	180	185	186	184	187	188	189	192	185	186	187	186	187	187	188	195	188	190	189	191	191	193	194	194	196
4444	587	F	178	188	186	189	190	190	180	185	182	185	182	189	200	189	180	188	187	195	186	191	185	192	186	191	193	193	186
4444	588	F	191	176	171	177	179	179	190	197	193	195	192	193	185	194	192	195	196	197	195	198	194	203	199	202	200	196	196
4444	589	F	179	184	178	182	183	180	184	188	183	189	178	187	183	186	181	188	186	193	186	192	185	191	186	192	191	192	187
4444	590	F	185	182	177	183	179	172	182	189	188		181	189	188	187	184	187	190	193	190	189	187	197	191	195	193	194	188
4444	591	F	173	171	168	173	174	172	171	177	174		172	178	177	178	174	180	176	182	176	182	178	188	182	189	185	187	180
4444	592	F	184	185	177	184	184	184	184	186	185	188	184	188	186	187	182	185	187	191	185	190	186	190	191	192	194	193	189
4444	593	F	184	184	180	187	184	181	184	182	186	189	181	186	188	187	186	184	187	191	187	187	191	195	192	197	195	194	191
4444	594	F	184	184	183	180	184	182	183	188	190	190	186	191	188	186	186	186	189	193	187	185	190	193	187	193	196	195	198
4444	595	F	182	182	181	177	187	184	184	187	189	191	186	191	191	192	189	192	192	197	193	194	188	197	195	197	200	199	192
4444	596	F	180	177	176	175	179	180	181	182	183	186	182	187	184	185	182	185	183	188	187	185	185	189	183	187	189	188	190
4444	597	F	175	173	173	176	176	177	179	183	179	183	179	184	182	178	179	183	180	184	179	183	177	188	185	190	190	191	184
4444	598	F	177	177	175	178	181	181	180	186	182	187	186	189	186	184	182	185	185	191	185	186	185	194	190	194	193	195	187

APPENDIX D: ANIMAL WEIGHTS AND SELECTED TISSUE WEIGHTS AT TIME OF SACRIFICE

EXPT NUMBER	CONCENTRATION OF Cu-Zn	ANIMAL NUMBER	SEX	SACRIFICE CODE	WEIGHT IN GRAMS ANIMAL	BRAIN	KIDNEYS	LIVER	LUNG	TESTES	OVARIES
4371	1.0 mg/m3	037	MALE	EOE	322.5	1.94	2.23	10.4	1.217	1.48	
4371	1.0 mg/m3	038	MALE	EOE	324.3	1.93	2.22	11.0	1.268	1.40	
4371	1.0 mg/m3	040	MALE	REC	298.1	1.88	1.95	8.1	1.158	1.33	
4371	1.0 mg/m3	043	MALE	EOE	311.2	1.93	1.84	9.0	1.359	1.47	
4371	1.0 mg/m3	044	MALE	EOE	299.0	1.96	1.92	9.8	1.479	1.50	
4371	1.0 mg/m3	046	MALE	EOE	325.4	1.93	2.08	9.6	1.332	1.43	
4371	1.0 mg/m3	048	MALE	REC	305.8	1.93	1.91	8.8	1.218	1.38	
4371	1.0 mg/m3	049	MALE	EOE	314.2	1.92	2.41	10.2	1.946	1.55	
4371	1.0 mg/m3	050	MALE	REC	340.0	1.95	2.21	10.8	1.206	1.36	
4371	1.0 mg/m3	051	MALE	REC	322.8	1.88	1.99	9.6	1.411	1.48	
4371	1.0 mg/m3	052	MALE	EOE	294.6	2.00	2.09	8.4	1.153	1.32	
4371	1.0 mn/m3	055	MALE	REC	313.3	1.93	1.90	8.8	1.198	1.39	
4371	1.0 mg/m3	056	MALE	REC	326.7	1.20	2.10	9.7	1.549	1.32	
4371	1.0 mg/m3	059	MALE	EOE	285.8	1.86	2.09	9.4	1.107	1.33	
4371	1.0 mg/m3	060	MALE	REC	343.9	1.91	2.20	10.5	1.204	1.09	
4371	1.0 mg/m3	061	MALE	EOE	311.9	1.87	2.16	9.8	1.284	0.90	
4371	1.0 mg/m3	062	MALE	REC	304.7	1.96	2.14	10.0	1.233	1.50	
4371	1.0 mg/m3	063	MALE	EOE	336.4	1.98	2.11	10.7	1.392	1.51	
4371	1.0 mg/m3	066	MALE	REC	331.0	1.90	2.28	10.9	1.263	1.47	
4371	1.0 mg/m3	067	MALE	REC	356.8	1.98	2.32	9.7	1.360	1.40	
4371	1.0 mg/m3	070	MALE	REC	334.8	1.88	2.38	10.1	1.292	1.50	
4371	1.0 mg/m3	072	MALE	EOE	309.3	1.94	2.08	10.2	1.230	1.38	
4371	1.0 mg/m3	537	FEMALE	EOE	187.0	1.76	1.47	5.4	1.066		0.022
4371	1.0 mg/m3	540	FEMALE	REC	188.7	1.78	1.55	6.3	0.987		0.050
4371	1.0 mg/m3	541	FEMALE	REC	188.2	1.81	1.37	5.3	0.864		0.074
4371	1.0 mg/m3	543	FEMALE	EOE	168.2	1.71	1.33	5.3	0.816		0.069
4371	1.0 mg/m3	544	FEMALE	REC	191.8	1.78	1.46	5.6	1.115		0.039
4371	1.0 mg/m3	547	FEMALE	EOE	194.5	1.88	1.54	5.9	1.045		0.067
4371	1.0 mg/m3	548	FEMALE	EOE	184.3	1.78	1.32	5.1	0.938		0.085
4371	1.0 mg/m3	549	FEMALE	EOE	195.0	1.76	1.57	5.7	0.944		0.059
4371	1.0 mg/m3	550	FEMALE	REC	195.0	1.75	1.38	5.6	1.038		0.051
4371	1.0 mg/m3	554	FEMALE	EOE	232.3	1.73	1.28	5.2	0.967		0.034
4371	1.0 mg/m3	555	FEMALE	REC	194.5	1.78	1.36	5.4	0.904		0.057
4371	1.0 mg/m3	556	FEMALE	REC	198.0	1.80	1.57	5.5	0.998		0.034
4371	1.0 mg/m3	558	FEMALE	REC	199.8	1.77	1.44	5.9	1.007		0.055
4371	1.0 mg/m3	560	FEMALE	REC	200.9	1.73	1.51	5.3	0.804		0.044

EXPT NUMBER	CONCENTRATION OF Cu-Zn	ANIMAL NUMBER	SEX	SACRIFICE CODE	WEIGHT IN GRAMS ANIMAL	BRAIN	KIDNEYS	LIVER	LUNG	TESTES	OVARIES
4371	1.0 mg/m3	562	FEMALE	REC	181.6	1.78	1.37	5.2	0.831		0.040
4371	1.0 mg/m3	563	FEMALE	REC	192.1	1.73	1.38	5.4	0.933		0.063
4371	1.0 mg/m3	564	FEMALE	EOE	190.2	1.79	1.38	5.2	0.884		0.059
4371	1.0 mg/m3	566	FEMALE	REC	182.9	1.77	1.33	4.9	0.890		0.048
4371	1.0 mg/m3	567	FEMALE	EOE	184.0	1.70	1.50	6.6	1.121		0.044
4371	1.0 mg/m3	569	FEMALE	EOE	182.3	1.76	1.37	5.2	0.988		0.091
4371	1.0 mg/m3	570	FEMALE	EOE	178.2	1.71	1.23	5.2	0.943		0.042
4371	1.0 mg/m3	571	FEMALE	EOE	187.7	1.70	1.25	5.3	0.931		0.053
4372	3.2 mg/m3	075	MALE	EOE	320.6	1.95	2.15	10.6	1.349	1.02	
4372	3.2 mg/m3	076	MALE	REC	356.5	1.96	2.21	11.0	1.294	1.52	
4372	3.2 mg/m3	079	MALE	REC	332.2	1.89	2.29	11.3	1.267	1.42	
4372	3.2 mg/m3	080	MALE	EOE	319.8	1.95	2.06	9.6	1.299	1.47	
4372	3.2 mg/m3	081	MALE	EOE	313.5	1.98	2.14	9.6	1.421	1.49	
4372	3.2 mg/m3	085	MALE	EOE	313.0	1.85	2.10	9.4	1.325	1.51	
4372	3.2 mg/m3	086	MALE	REC	330.6	1.91	2.21	10.2	1.376	1.61	
4372	3.2 mg/m3	087	MALE	EOE	330.6	1.89	2.23	10.7	1.574	1.25	
4372	3.2 mg/m3	089	MALE	REC	328.5	1.86	2.39	10.3	1.307	1.39	
4372	3.2 mg/m3	090	MALE	EOE	322.1	1.90	2.08	10.2	1.153	1.47	
4372	3.2 mg/m3	092	MALE	REC	365.4	1.92	2.57	11.7	1.384	1.44	
4372	3.2 mg/m3	093	MALE	REC	331.5	1.91	2.14	10.3	1.384	1.50	
4372	3.2 mg/m3	095	MALE	REC	323.2	1.90	2.20	9.8	1.283	1.42	
4372	3.2 mg/m3	096	MALE	REC	329.7	1.89	2.04	9.5	1.155	1.33	
4372	3.2 mg/m3	100	MALE	EOE	323.1	1.83	1.99	9.8	1.381	1.32	
4372	3.2 mg/m3	101	MALE	EOE	310.9	1.88	2.01	9.5	1.403	1.45	
4372	3.2 mg/m3	102	MALE	REC	323.3	1.82	2.22	11.1	1.212	1.34	
4372	3.2 mg/m3	103	MALE	EOE	285.6	1.94	1.93	8.6	1.382	1.40	
4372	3.2 mg/m3	104	MALE	EOE	298.6	1.85	2.24	9.8	1.339	1.41	
4372	3.2 mg/m3	109	MALE	EOE	303.1	1.89	2.34	9.0	1.345	1.42	
4372	3.2 mg/m3	111	MALE	REC	330.6	1.87	2.02	9.0	1.383	1.28	
4372	3.2 mg/m3	112	MALE	REC	338.5	1.90	2.16	10.2	1.335	1.04	
4372	3.2 mg/m3	575	FEMALE	EOE	199.4	1.76	1.38	5.7	1.021		0.046
4372	3.2 mg/m3	576	FEMALE	REC	192.2	1.79	1.40	5.5	0.978		0.051
4372	3.2 mg/m3	578	FEMALE	REC	189.3	1.74	1.30	5.4	0.890		0.045
4372	3.2 mg/m3	579	FEMALE	REC	213.7	1.71	1.73	6.5	1.025		0.072
4372	3.2 mg/m3	580	FEMALE	EOE	183.0	1.71	1.38	5.4	1.005		0.039
4372	3.2 mg/m3	584	FEMALE	REC	197.5	1.72	1.52	5.2	1.012		0.043
4372	3.2 mg/m3	585	FEMALE	REC	207.2	1.82	1.59	6.4	0.936		0.065
4372	3.2 mg/m3	588	FEMALE	EOE	182.9	1.74	1.37	5.2	0.955		0.041
4372	3.2 mg/m3	590	FEMALE	EOE	192.8	1.79	1.42	6.0	1.166		0.056

EXPT NUMBER	CONCENTRATION OF Cu-Zn	ANIMAL NUMBER	SEX	SACRIFICE CODE	WEIGHT IN GRAMS						
					ANIMAL	BRAIN	KIDNEYS	LIVER	LUNG	TESTES	OVARIES
4372	3.2 mg/m3	591	FEMALE	REC	213.7	1.77	1.53	5.6	0.983		0.056
4372	3.2 mg/m3	592	FEMALE	EOE	180.0	1.75	1.40	5.2	1.195		0.054
4372	3.2 mg/m3	593	FEMALE	EOE	186.1	1.67	1.42	5.5	1.104		0.033
4372	3.2 mg/m3	598	FEMALE	REC	206.3	1.79	1.40	5.9	0.941		0.042
4372	3.2 mg/m3	599	FEMALE	EOE	191.8	1.78	1.44	5.3	1.061		0.066
4372	3.2 mg/m3	600	FEMALE	REC	189.9	1.75	1.44	5.3	0.923		0.035
4372	3.2 mg/m3	602	FEMALE	REC	189.0	1.76	1.42	5.4	1.026		0.060
4372	3.2 mg/m3	603	FEMALE	EOE		1.82	1.39	5.8	1.006		0.050
4372	3.2 mg/m3	604	FEMALE	REC	184.4	1.71	1.31	5.7	0.863		0.058
4372	3.2 mg/m3	605	FEMALE	EOE	182.7	1.71	1.34	5.3	0.975		0.042
4372	3.2 mg/m3	606	FEMALE	REC	195.5	1.77	1.42	5.9	0.970		0.075
4372	3.2 mg/m3	608	FEMALE	EOE	184.9	1.76	1.33	5.5	0.968		0.044
4372	3.2 mg/m3	609	FEMALE	EOE	193.7	1.82	1.40	5.7	1.231		0.062
4373	10 mg/m3	114	MALE	EOE	299.2	1.90	2.13	10.1	1.810	1.36	
4373	10 mg/m3	116	MALE	REC		1.87	2.80	8.6	1.593	1.44	
4373	10 mg/m3	117	MALE	REC	328.8	1.94	2.25	9.7	1.410	1.36	
4373	10 mg/m3	119	MALE	REC	317.4	1.96	2.19	10.9	1.390	1.34	
4373	10 mg/m3	122	MALE	REC	360.1	1.91	2.25	11.4	1.568	1.47	
4373	10 mg/m3	125	MALE	EOE	302.6	1.80	2.13	9.8	1.431	1.49	
4373	10 mg/m3	126	MALE	EOE	291.9	1.88	2.04	9.2	1.661	1.46	
4373	10 mg/m3	127	MALE	REC	322.6	1.92	2.25	10.7	1.300	1.39	
4373	10 mg/m3	128	MALE	EOE	304.9	1.93	2.20	9.7	1.598	1.46	
4373	10 mg/m3	130	MALE	EOE	294.7	1.83	1.91	9.4	1.604	1.21	
4373	10 mg/m3	132	MALE	EOE	283.1	1.81	1.91	9.1	1.443	1.36	
4373	10 mg/m3	133	MALE	EOE	289.9	1.94	2.06	9.7	1.482	1.35	
4373	10 mg/m3	134	MALE	REC	335.2	1.94	2.27	10.8	1.550	1.40	
4373	10 mg/m3	135	MALE	REC	324.1	1.88	2.22	10.5	1.434	1.45	
4373	10 mg/m3	136	MALE	EOE	293.1	1.94	2.04	9.3	1.515	1.32	
4373	10 mg/m3	140	MALE	EOE	284.0	1.80	1.90	8.5	1.336	1.41	
4373	10 mg/m3	141	MALE	EOE	312.0	1.89	2.16	9.8	1.520	1.46	
4373	10 mg/m3	142	MALE	EOE	304.8	1.91	2.04	10.2	1.649	1.39	
4373	10 mg/m3	144	MALE	REC	330.2	1.89	2.29	10.1	1.542	1.45	
4373	10 mg/m3	147	MALE	REC	323.5	1.87	2.04	9.3	1.451	1.44	
4373	10 mg/m3	148	MALE	REC	329.0	1.87	2.04	9.7	1.254	1.46	
4373	10 mg/m3	149	MALE	REC	322.4	1.91	2.02	9.2	1.455	1.25	
4373	10 mg/m3	615	FEMALE	EOE	182.6	1.76	1.42	5.4	1.156		0.074
4373	10 mg/m3	616	FEMALE	REC	192.1	1.75	1.45	6.3	0.930		0.055
4373	10 mg/m3	617	FEMALE	EOE	182.5	1.76	1.45	5.6	1.104		0.045
4373	10 mg/m3	618	FEMALE	REC	185.1	1.75	1.40	5.4	0.994		0.059

EXPT NUMBER	CONCENTRATION OF Cu-Zn	ANIMAL NUMBER	SEX	SACRIFICE CODE	WEIGHT IN GRAMS ANIMAL	BRAIN	KIDNEYS	LIVER	LUNG	TESTES	OVARIES
4373	10 mg/m3	620	FEMALE	EOE	186.1	1.74	1.39	5.8	1.305		0.054
4373	10 mg/m3	624	FEMALE	REC	192.8	1.75	1.38	5.3	1.082		0.051
4373	10 mg/m3	625	FEMALE	EOE	191.9	1.74	1.44	5.6	1.155		0.051
4373	10 mg/m3	626	FEMALE	REC	199.5	1.78	1.50	5.7	1.120		0.038
4373	10 mg/m3	627	FEMALE	REC	188.8	1.49	1.45	5.8	1.062		0.068
4373	10 mg/m3	628	FEMALE	EOE	175.0	1.79	1.43	5.5	1.166		0.081
4373	10 mg/m3	630	FEMALE	EOE	187.5	1.72	1.35	5.3	1.156		0.050
4373	10 mg/m3	631	FEMALE	REC	189.0	1.79	1.36	5.1	1.056		0.036
4373	10 mg/m3	632	FEMALE	EOE	179.6	1.72	1.31	5.4	1.011		0.058
4373	10 mg/m3	633	FEMALE	EOE	178.3	1.77	1.26	5.3	1.158		0.047
4373	10 mg/m3	634	FEMALE	REC	199.8	1.74	1.42	5.2	1.050		0.037
4373	10 mg/m3	636	FEMALE	EOE	197.0	1.76	1.42	6.0	1.184		0.048
4373	10 mg/m3	638	FEMALE	EOE	176.5	1.67	1.35	5.3	1.087		0.043
4373	10 mg/m3	639	FEMALE	REC	197.7	1.78	1.37	5.4	0.994		0.038
4373	10 mg/m3	642	FEMALE	REC	174.3	1.70	1.22	4.3	0.821		0.052
4373	10 mg/m3	643	FEMALE	EOE	175.4	1.75	1.44	5.2	1.041		0.057
4373	10 mg/m3	648	FEMALE	REC	181.4	1.78	1.32	5.3	0.950		0.038
4373	10 mg/m3	650	FEMALE	REC	184.3	1.78	1.45	5.5	0.960		0.058
4442	0 (SHAM)	109	MALE	REC	380.7	2.04	2.86	12.3	1.499	1.55	
4442	0 (SHAM)	110	MALE	REC	372.5	2.00	2.45	12.2	1.394	1.52	
4442	0 (SHAM)	111	MALE	EOE	315.0	1.90	2.24	8.8	1.267	1.36	
4442	0 (SHAM)	112	MALE	EOE	331.0	1.94	1.94	9.9	1.293	1.47	
4442	0 (SHAM)	114	MALE	REC	362.3	1.97	2.64	12.0	1.196	1.48	
4442	0 (SHAM)	115	MALE	EOE	339.6	1.98	2.33	11.6	1.464	1.52	
4442	0 (SHAM)	116	MALE	EOE	325.0	1.84	2.07	9.8	1.501	1.44	
4442	0 (SHAM)	118	MALE	REC	338.5	1.95	2.41	10.9	1.515	1.38	
4442	0 (SHAM)	119	MALE	EOE	321.2	1.99	2.26	9.1	1.408	1.37	
4442	0 (SHAM)	120	MALE	EOE	333.5	1.88	2.32	10.7	1.332	1.25	
4442	0 (SHAM)	121	MALE	REC	364.1	1.93	2.45	13.2	1.632	1.92	
4442	0 (SHAM)	122	MALE	EOE	336.2	1.92	2.16	11.3	1.498	1.09	
4442	0 (SHAM)	123	MALE	REC	352.1	2.00	2.15	11.6	1.539	1.44	
4442	0 (SHAM)	127	MALE	EOE	338.0	1.95	2.20	10.1	1.514	1.58	
4442	0 (SHAM)	128	MALE	EOE	328.9	1.98	2.39	11.0	1.351	1.48	
4442	0 (SHAM)	130	MALE	REC	384.8	2.00	2.74	13.1	1.459	1.50	
4442	0 (SHAM)	131	MALE	REC	336.5	1.99	2.30	11.3	1.620	1.45	
4442	0 (SHAM)	132	MALE	REC	392.0	2.04	2.38	12.6	1.490	1.52	
4442	0 (SHAM)	134	MALE	REC	374.1	2.00	2.48	11.7	1.697	1.60	
4442	0 (SHAM)	136	MALE	EOE	341.3	1.89	2.24	10.8	1.432	1.50	

EXPT NUMBER	CONCENTRATION OF Cu-Zn	ANIMAL NUMBER	SEX	SACRIFICE CODE	WEIGHT IN GRAMS: ANIMAL	BRAIN	KIDNEYS	LIVER	LUNG	TESTES	OVARIES
4442	0 (SHAM)	137	MALE	REC	375.4	2.02	2.52	11.5	1.467	1.42	
4442	0 (SHAM)	138	MALE	EOE	333.0	1.91	2.11	9.5	1.569	1.49	
4442	0 (SHAM)	509	FEMALE	EOE	193.9	1.78	1.31	5.8	0.955		0.082
4442	0 (SHAM)	510	FEMALE	REC	204.6	1.75	1.39	6.1	1.198		0.048
4442	0 (SHAM)	511	FEMALE	REC	201.6	1.79	1.52	5.9	1.020		0.053
4442	0 (SHAM)	512	FEMALE	REC	192.1	1.80	1.45	6.2	1.053		0.061
4442	0 (SHAM)	513	FEMALE	REC	213.4	1.79	1.54	6.1	1.123		0.064
4442	0 (SHAM)	515	FEMALE	REC	206.1	1.81	0.70	6.1	1.042		0.057
4442	0 (SHAM)	516	FEMALE	REC	210.1	1.85	1.57	6.8	1.251		0.062
4442	0 (SHAM)	517	FEMALE	EOE	199.2	2.03	1.38	5.8	1.204		0.068
4442	0 (SHAM)	518	FEMALE	REC	216.2	1.79	1.58	7.5	1.021		0.078
4442	0 (SHAM)	519	FEMALE	EOE	200.0	1.81	1.51	5.8	1.037		0.050
4442	0 (SHAM)	520	FEMALE	EOE	190.1	1.75	1.41	5.3	1.058		0.046
4442	0 (SHAM)	522	FEMALE	REC	205.0	1.83	1.60	6.6	1.043		0.078
4442	0 (SHAM)	523	FEMALE	REC	206.3	1.80	1.57	6.2	1.003		0.061
4442	0 (SHAM)	524	FEMALE	EOE	191.2	1.71	1.44	5.8	0.933		0.048
4442	0 (SHAM)	526	FEMALE	EOE	188.5	1.76	1.42	5.4	0.962		0.056
4442	0 (SHAM)	527	FEMALE	EOE	198.7	1.78	1.39	6.4	1.108		0.049
4442	0 (SHAM)	530	FEMALE	REC	200.9	1.81	1.57	6.4	0.931		0.060
4442	0 (SHAM)	531	FEMALE	EOE	200.7	1.77	1.34	6.1	1.043		0.041
4442	0 (SHAM)	532	FEMALE	EOE	196.1	1.83	1.38	5.7	1.060		0.058
4442	0 (SHAM)	533	FEMALE	EOE	190.7	1.76	1.27	5.5	0.970		0.043
4442	0 (SHAM)	535	FEMALE	REC	207.6	1.77	1.47	6.4	1.038		0.053
4442	0 (SHAM)	538	FEMALE	EOE	191.4	1.71	1.45	5.9	1.183		0.051
4443	0.32 mg/m3	139	MALE	REC	357.1	1.98	2.48	12.1	1.553	1.56	
4443	0.32 mg/m3	140	MALE	REC	364.2	1.98	2.38	12.4	1.699	2.26	
4443	0.32 mg/m3	141	MALE	EOE	344.0	1.94	2.10	10.6	1.589	1.48	
4443	0.32 mg/m3	142	MALE	REC	376.0	1.99	1.16	12.5	1.169	1.44	
4443	0.32 mg/m3	143	MALE	REC	357.8	1.92	2.34	11.4	1.526	2.06	
4443	0.32 mg/m3	144	MALE	EOE	328.2	1.90	2.29	10.2		1.51	
4443	0.32 mg/m3	145	MALE	EOE	328.7	1.87	2.05	10.7	1.536	1.43	
4443	0.32 mg/m3	146	MALE	EOE	338.1	1.96	2.26	10.6	1.475	1.53	
4443	0.32 mg/m3	147	MALE	REC	370.1	1.98	2.60	12.2	1.343	1.59	
4443	0.32 mg/m3	148	MALE	EOE	337.2	1.84	1.98	10.1	1.349	1.47	
4443	0.32 mg/m3	149	MALE	EOE	315.6	1.88	2.18	9.8	1.473	1.44	
4443	0.32 mg/m3	150	MALE	REC	329.8	1.95	2.19	8.7	1.348	1.51	
4443	0.32 mg/m3	151	MALE	REC	367.7	1.99	2.36	12.0	1.536	1.49	
4443	0.32 mg/m3	152	MALE	REC	375.8	1.90	2.29	11.5	1.931		
4443	0.32 mg/m3	153	MALE	EOE	333.8	1.95	2.21	10.4	1.476	1.49	

EXPT NUMBER	CONCENTRATION OF Cu-Zn	ANIMAL NUMBER	SEX	SACRIFICE CODE	WEIGHT IN GRAMS ANIMAL	BRAIN	KIDNEYS	LIVER	LUNG	TESTES	OVARIES
4443	0.32 mg/m3	154	MALE	EOE	324.4	1.81	2.10	10.1	1.545	1.50	
4443	0.32 mg/m3	155	MALE	REC	350.7	1.93	2.37	11.8	1.655	1.93	
4443	0.32 mg/m3	156	MALE	EOE	340.7	1.89	2.10	10.7	1.214	1.44	
4443	0.32 mg/m3	157	MALE	EOE	354.0	1.89	2.26	10.9	1.554	1.48	
4443	0.32 mg/m3	158	MALE	REC	361.8	1.93	2.08	11.9	1.314	1.70	
4443	0.32 mg/m3	159	MALE	EOE	327.6	1.92	2.12	10.2	1.365	1.51	
4443	0.32 mg/m3	160	MALE	REC	323.3	1.94	2.01	10.1		1.51	
4443	0.32 mg/m3	539	FEMALE	REC	203.5	1.77	1.49	6.8	1.222		0.074
4443	0.32 mg/m3	540	FEMALE	EOE	193.9	1.75	1.45	6.6	0.984		0.038
4443	0.32 mg/m3	541	FEMALE	REC	190.5	1.77	0.65	6.1	0.896		0.068
4443	0.32 mg/m3	542	FEMALE	EOE	207.5	1.80	1.49	5.8	0.923		0.066
4443	0.32 mg/m3	543	FEMALE	REC	206.3	1.86	1.64	6.7	1.217		0.089
4443	0.32 mg/m3	544	FEMALE	EOE	196.2	1.71	1.35	5.5	0.972		0.041
4443	0.32 mg/m3	545	FEMALE	REC	220.7	1.80	1.55	6.7	0.970		0.048
4443	0.32 mg/m3	546	FEMALE	EOE	193.0	1.73	1.34	5.5	1.027		0.050
4443	0.32 mg/m3	547	FEMALE	EOE	183.9	1.72	1.40	5.1	0.951		0.053
4443	0.32 mg/m3	548	FEMALE	REC	216.8	1.82	1.40	6.5	1.014		0.050
4443	0.32 mg/m3	549	FEMALE	EOE	200.1	1.78	1.34	5.5	1.019		0.079
4443	0.32 mg/m3	550	FEMALE	REC	204.1	1.77	1.46	6.1	1.066		0.048
4443	0.32 mg/m3	551	FEMALE	EOE	208.3	1.70	1.51	6.4	0.920		0.052
4443	0.32 mg/m3	552	FEMALE	REC	204.6	1.81	1.38	6.2	0.963		0.067
4443	0.32 mg/m3	553	FEMALE	REC	207.1	1.81	1.49	6.7	1.145		0.050
4443	0.32 mg/m3	554	FEMALE	REC	201.0	1.77	1.56	5.7	1.156		0.080
4443	0.32 mg/m3	555	FEMALE	EOE	192.4	1.69	1.32	5.4	0.834		0.044
4443	0.32 mg/m3	556	FEMALE	REC	198.5	1.83	1.53	6.4	0.853		0.060
4443	0.32 mg/m3	557	FEMALE	REC	206.7	1.84	1.53	6.5	1.018		0.060
4443	0.32 mg/m3	558	FEMALE	EOE	194.6	1.80	1.54	6.1	1.039		0.051
4443	0.32 mg/m3	559	FEMALE	EOE	191.5	1.73	1.31	5.9	0.953		0.037
4443	0.32 mg/m3	560	FEMALE	EOE	187.1	1.68	1.32	6.0	1.314		0.041
4444	3.2 mg/m3	170	MALE	REC	368.5	1.95	2.24	11.5	1.662	1.65	
4444	3.2 mg/m3	171	MALE	REC	332.4	2.11	2.27	10.9	1.311	1.52	
4444	3.2 mg/m3	173	MALE	REC	365.8	1.91	2.37	12.9	1.621	2.34	
4444	3.2 mg/m3	174	MALE	REC	351.3	1.97	2.40	11.1	1.518	1.62	
4444	3.2 mg/m3	175	MALE	EOE	344.2	1.89	2.16	10.8	1.388	1.68	
4444	3.2 mg/m3	177	MALE	REC	366.7	1.93	2.26	11.4	1.666	2.19	
4444	3.2 mg/m3	179	MALE	REC	378.8	2.05	2.63	11.7	1.507	1.33	
4444	3.2 mg/m3	180	MALE	EOE	325.5	1.86	2.03	9.9	1.402	1.44	
4444	3.2 mg/m3	181	MALE	EOE	329.3	1.89	2.22	10.8	1.406	1.52	
4444	3.2 mg/m3	182	MALE	EOE	323.8	1.91	2.30	11.1	1.488	1.53	

EXPT NUMBER	CONCENTRATION OF Cu-Zn	ANIMAL NUMBER	SEX	SACRIFICE CODE	WEIGHT IN GRAMS						
					ANIMAL	BRAIN	KIDNEYS	LIVER	LUNG	TESTES	OVARIES
4444	3.2 mg/m3	184	MALE	REC	356.3	2.01	2.39	11.5	1.542	1.51	
4444	3.2 mg/m3	185	MALE	EOE	323.5	1.89	2.34	9.0	1.407	1.54	
4444	3.2 mg/m3	186	MALE	REC	359.1	1.97	2.52	11.3	1.636	1.55	
4444	3.2 mg/m3	187	MALE	EOE	334.3	1.88	2.20	9.8	1.257	1.47	
4444	3.2 mg/m3	188	MALE	REC	357.9	1.92	2.24	11.4	1.380	1.58	
4444	3.2 mg/m3	189	MALE	EOE	329.7	1.98	2.48	10.3	1.896	1.67	
4444	3.2 mg/m3	190	MALE	EOE		1.94	2.18	9.8	1.279	1.58	
4444	3.2 mg/m3	191	MALE	EOE	314.8	1.90	2.06	8.7	1.235	1.54	
4444	3.2 mg/m3	192	MALE	EOE	332.2	1.94	2.12	10.9	1.842	1.52	
4444	3.2 mg/m3	195	MALE	REC	366.8	1.94	1.19	11.7	1.359	1.50	
4444	3.2 mg/m3	196	MALE	REC	370.2	1.94	2.58	12.8	1.557	1.58	
4444	3.2 mg/m3	197	MALE	EOE	330.9	1.91	2.02	10.5	1.552	1.28	
4444	3.2 mg/m3	569	FEMALE	REC	208.5	1.80	1.51	6.1	1.150		0.069
4444	3.2 mg/m3	570	FEMALE	REC	196.0	1.87	1.47	5.8	1.093		0.064
4444	3.2 mg/m3	573	FEMALE	EOE	184.1	1.74	1.37	5.3	1.093		0.071
4444	3.2 mg/m3	574	FEMALE	EOE	195.9	1.73	1.34	5.6	0.938		0.054
4444	3.2 mg/m3	575	FEMALE	REC	197.2	1.92	1.52	6.1	1.235		0.083
4444	3.2 mg/m3	576	FEMALE	REC	204.0	1.86	1.47	6.2	1.091		0.043
4444	3.2 mg/m3	577	FEMALE	REC	205.4	1.78	1.54	6.5	0.989		0.060
4444	3.2 mg/m3	578	FEMALE	EOE	187.3	1.70	1.32	5.2	0.907		0.058
4444	3.2 mg/m3	580	FEMALE	REC	204.4	1.84	1.34	6.4	1.003		0.061
4444	3.2 mg/m3	581	FEMALE	EOE	193.1	1.79	1.46	6.4	1.072		0.048
4444	3.2 mg/m3	582	FEMALE	REC	210.1	1.83	1.55	6.9	1.110		0.055
4444	3.2 mg/m3	583	FEMALE	EOE	195.8	1.73	1.49	6.3	0.984		0.060
4444	3.2 mg/m3	585	FEMALE	REC	205.0	1.77	1.61	6.5	0.960		0.053
4444	3.2 mg/m3	586	FEMALE	EOE	199.4	1.82	1.32	5.5	1.057		0.043
4444	3.2 mg/m3	588	FEMALE	EOE	202.7	1.78	1.38	5.8	1.080		0.052
4444	3.2 mg/m3	589	FEMALE	EOE	195.5	1.72	1.32	5.7	1.048		0.057
4444	3.2 mg/m3	590	FEMALE	EOE	198.5	1.77	1.38	6.0	1.171		0.052
4444	3.2 mg/m3	591	FEMALE	REC	196.7	1.82	1.51	6.5	1.470		0.076
4444	3.2 mg/m3	592	FEMALE	REC	201.5	1.85	1.56	5.9	1.026		0.045
4444	3.2 mg/m3	594	FEMALE	EOE	195.4	1.75	1.45	5.7	1.092		0.077
4444	3.2 mg/m3	595	FEMALE	REC	206.0	1.82	1.50	6.5	0.995		0.063
4444	3.2 mg/m3	596	FEMALE	EOE	189.5	1.74	1.40	5.4	1.141		0.075

APPENDIX E. ENDPOINT EVALUATION RESULTS FOR INDIVIDUAL ANIMALS (HEMATOLOGY, CHEMISTRY, IMMUNOLOGY, PHAGOCYTOSIS)

1. HEMATOLOGY DATA

CONCENTRATION OF Cu-Zn	EXPT NUMBER	ANIMAL NUMBER	ANIMAL SEX	SACRIFICE CODE	RBC	HEMA	HGB	MCV	MCHV	BWBC	SEGM	EOSI	LYMP	MONO	NRBC
1.0 mg/m3	4371	038	MALE	EOE	7.98	41.9	15.0	53	35.8	2.0	20	2	78	0	4
1.0 mg/m3	4371	046	MALE	EOE	8.10	41.8	15.2	52	36.4	4.5	18	1	80	1	0
1.0 mg/m3	4371	050	MALE	REC	7.94	40.4	15.5	51	38.4	4.7	30	1	67	2	9
1.0 mg/m3	4371	051	MALE	REC	8.26	42.4	15.6	52	36.8	4.6	31	2	66	1	7
1.0 mg/m3	4371	052	MALE	EOE	8.09	42.2	15.1	53	35.8	2.8	15	3	82	0	0
1.0 mg/m3	4371	055	MALE	REC	8.06	42.3	16.3	53	38.5	4.4	19	5	76	0	5
1.0 mg/m3	4371	056	MALE	REC	7.94	40.6	15.8	52	38.9	4.3	29	1	68	2	1
1.0 mg/m3	4371	059	MALE	EOE	7.89	40.7	14.6	52	35.9	3.7	25	1	73	1	1
1.0 mg/m3	4371	060	MALE	REC	8.17	41.7	16.0	52	38.4	3.6	36	3	60	1	4
1.0 mg/m3	4371	061	MALE	EOE	8.16	42.2	15.4	52	36.5	4.1	43	2	55	0	0
1.0 mg/m3	4371	547	FEMALE	EOE	7.45	41.5	14.9	57	35.9	2.8	16	3	79	2	3
1.0 mg/m3	4371	548	FEMALE	EOE	7.41	41.2	14.7	56	35.7	3.0	16	0	82	2	6
1.0 mg/m3	4371	550	FEMALE	REC	7.81	42.3	16.0	55	37.8	4.6	31	4	63	2	9
1.0 mg/m3	4371	554	FEMALE	EOE	7.69	40.4	14.9	53	36.9	2.9	16	1	83	1	7
1.0 mg/m3	4371	555	FEMALE	REC	7.37	39.6	15.5	54	39.1	3.6	20	1	77	2	4
1.0 mg/m3	4371	560	FEMALE	REC	7.23	39.0	15.4	55	39.5	4.7	19	1	79	1	1
1.0 mg/m3	4371	562	FEMALE	REC	7.66	41.5	15.8	55	38.1	4.3	31	1	68	0	7
1.0 mg/m3	4371	563	FEMALE	REC	7.96	42.5	16.2	54	38.1	5.0	14	2	83	1	9
1.0 mg/m3	4371	570	FEMALE	EOE	7.71	41.7	15.3	55	36.7	4.0	35	1	63	1	6
1.0 mg/m3	4371	571	FEMALE	EOE	7.64	42.4	15.1	56	35.6	3.5	11	1	87	1	3
3.2 mg/m3	4372	075	MALE	EOE	8.18	42.7	15.3	53	35.8	3.1	30	1	68	1	0
3.2 mg/m3	4372	081	MALE	EOE	8.30	42.3	15.6	52	36.9	3.5	20	1	77	2	1
3.2 mg/m3	4372	085	MALE	EOE	7.87	40.3	15.2	52	37.7	3.2	25	1	74	0	1
3.2 mg/m3	4372	086	MALE	REC	8.01	40.9	15.9	52	38.9	4.8	42	1	56	1	4
3.2 mg/m3	4372	090	MALE	EOE	7.76	39.5	14.7	52	37.2	3.7	39	1	59	1	7
3.2 mg/m3	4372	092	MALE	REC	8.42	42.6	16.3	51	38.3	5.0	31	1	67	1	8
3.2 mg/m3	4372	096	MALE	REC	7.59	39.0	15.6	52	40.0	4.9	34	0	64	2	5
3.2 mg/m3	4372	100	MALE	EOE	7.90	40.6	14.9	52	36.7	3.9	36	2	62	0	3

CONCENTRATION OF Cu-Zn	EXPT NUMBER	ANIMAL NUMBER	ANIMAL SEX	SACRIFICE CODE	RBC	HEMA	HGB	MCV	MCHV	BWBC	SEGM	EOSI	LYMP	MONO	NRBC
3.2 mg/m3	4372	111	MALE	REC	7.62	39.5	15.6	52	39.5	5.4	22	3	69	6	4
3.2 mg/m3	4372	112	MALE	REC	8.15	41.5	16.1	52	38.8	6.5	16	1	81	2	3
3.2 mg/m3	4372	576	FEMALE	REC	7.41	39.5	15.2	54	38.5	3.3	13	0	86	1	1
3.2 mg/m3	4372	585	FEMALE	REC	7.80	42.0	15.8	55	37.6	3.1	21	2	75	2	2
3.2 mg/m3	4372	590	FEMALE	EOE	7.69	42.0	15.4	55	36.7	1.2	22	1	77	0	3
3.2 mg/m3	4372	598	FEMALE	REC	7.79	42.4	16.2	55	38.2	7.4	38	3	57	2	4
3.2 mg/m3	4372	599	FEMALE	EOE	7.43	41.2	15.0	56	36.4	3.3	10	2	88	0	0
3.2 mg/m3	4372	602	FEMALE	REC	7.46	38.4	14.9	52	38.8	4.9	22	0	77	1	2
3.2 mg/m3	4372	603	FEMALE	EOE	7.87	43.3	15.5	56	35.8	3.3	25	1	74	0	0
3.2 mg/m3	4372	606	FEMALE	REC	7.57	41.3	15.4	55	37.3	5.1	22	1	77	0	1
3.2 mg/m3	4372	608	FEMALE	EOE	7.92	44.3	16.1	57	36.3	3.8	22	1	76	0	1
3.2 mg/m3	4372	609	FEMALE	EOE	6.73	36.7	13.5	55	36.8	3.5	27	1	72	0	1
10 mg/m3	4373	122	MALE	REC	7.80	39.2	15.5	51	39.5	2.8	21	0	79	0	5
10 mg/m3	4373	127	MALE	REC	8.03	40.5	15.5	51	38.3	4.1	22	2	76	0	0
10 mg/m3	4373	128	MALE	EOE	8.06	42.3	15.5	53	36.6	5.3	20	1	78	1	7
10 mg/m3	4373	130	MALE	EOE	7.95	40.7	14.9	52	36.6	3.2	33	2	64	1	1
10 mg/m3	4373	134	MALE	REC	8.31	42.1	15.9	51	37.8	4.8	48	1	49	2	4
10 mg/m3	4373	135	MALE	REC	8.19	41.5	15.9	51	38.3	3.8	27	4	64	5	1
10 mg/m3	4373	136	MALE	EOE	8.37	43.5	16.0	53	36.8	3.9	35	1	62	2	3
10 mg/m3	4373	141	MALE	EOE	7.67	39.3	14.5	52	36.9	3.1	37	3	60	0	8
10 mg/m3	4373	142	MALE	EOE	8.11	41.4	15.3	52	37.0	5.4	26	0	72	2	2
10 mg/m3	4373	149	MALE	REC	8.05	41.2	16.3	52	39.6	5.2	35	2	62	1	7
10 mg/m3	4373	615	FEMALE	EOE	7.37	41.3	15.0	57	36.3	3.9	30	1	68	1	1
10 mg/m3	4373	616	FEMALE	REC	7.08	37.8	15.2	54	40.2	1.7	17	1	81	1	5
10 mg/m3	4373	627	FEMALE	REC	7.45	39.4	15.5	54	39.3	4.8	27	3	67	3	0
10 mg/m3	4373	628	FEMALE	EOE	7.82	43.1	15.8	56	36.7	5.0	28	0	69	3	9
10 mg/m3	4373	632	FEMALE	EOE	7.58	40.7	15.3	55	37.6	1.2	36	2	61	1	1
10 mg/m3	4373	633	FEMALE	EOE	7.84	43.5	15.8	56	36.3	5.7	34	1	62	3	3
10 mg/m3	437	639	FEMALE	REC	7.11	37.7	15.1	54	10.1	3.1	20	8	70	2	6
10 mg/m3	437	642	FEMALE	REC	7.35	39.3	15.5	54	39.4	2.8	16	3	79	2	0
10 mg/m3	4373	643	FEMALE	EOE	7.64	41.0	15.1	54	36.8	3.6	33	2	63	1	3
10 mg/m3	4373	650	FEMALE	REC	7.36	39.4	15.1	54	38.3	3.6	20	2	77	1	6

2. SERUM CHEMISTRY DATA

CONCENTRATION OF Cu-Zn	EXPT NUMBER	ANIMAL NUMBER	ANIMAL SEX	SACRIFICE CODE	ALKP	SGPT	BUN	TBIL	TPRO	ALB
1.0 mg/m3	4371	038	MALE	EOE	90.0	51.6	19.8	0.3	6.8	4.7
1.0 mg/m3	4371	046	MALE	EOE	85.2	44.2	25.5	0.2	5.7	4.6
1.0 mg/m3	4371	050	MALE	REC	90.6	49.5	21.9	0.1	6.7	4.4
1.0 mg/m3	4371	051	MALE	REC	76.7	42.2	25.5	0.2	6.3	4.4
1.0 mg/m3	4371	052	MALE	EOE	82.2	42.7	18.0	0.2	5.3	3.8
1.0 mg/m3	4371	055	MALE	REC	79.2	55.9	25.8	0.0	5.7	4.6
1.0 mg/m3	4371	056	MALE	REC	73.0	59.2	22.4	0.1	5.9	4.4
1.0 mg/m3	4371	059	MALE	EOE	80.0	35.2	30.7	0.0	6.6	4.8
1.0 mg/m3	4371	060	MALE	REC	88.0	52.1	22.1	0.2	6.4	4.3
1.0 mg/m3	4371	061	MALE	EOE	83.4	37.9	27.4	0.1	6.4	4.8
1.0 mg/m3	4371	547	FEMALE	EOE	91.8	35.3	23.2	0.1	6.8	4.9
1.0 mg/m3	4371	548	FEMALE	EOE	97.2	37.5	22.4	0.1	6.5	5.0
1.0 mg/m3	4371	550	FEMALE	REC	77.8	38.6	21.6	0.2	5.9	4.9
1.0 mg/m3	4371	554	FEMALE	EOE	86.7	41.8	23.9	0.2	7.6	5.5
1.0 mg/m3	4371	555	FEMALE	REC	72.5	43.8	25.6	0.2	6.4	4.8
1.0 mg/m3	4371	560	FEMALE	REC	64.9	37.0	21.6	0.2	5.6	4.2
1.0 mg/m3	4371	562	FEMALE	REC	79.7	41.4	23.7	0.2	5.6	4.5
1.0 mg/m3	4371	563	FEMALE	REC	75.4	41.6	24.1	0.2	5.8	4.8
1.0 mg/m3	4371	570	FEMALE	EOE	98.8	71.1	22.8	0.2	6.3	5.0
1.0 mg/m3	4371	571	FEMALE	EOE	82.8	33.7	31.3	0.2	5.4	4.4
3.2 mg/m3	4372	075	MALE	EOE	80.1	49.6	26.7	0.1	5.7	4.3
3.2 mg/m3	4372	081	MALE	EOE	95.2	40.3	18.9	0.0	6.1	4.7
3.2 mg/m3	4372	085	MALE	EOE	72.1	40.7	22.1	0.1	6.3	5.6
3.2 mg/m3	4372	086	MALE	REC	96.0	48.1	24.1	0.2	6.1	4.7
3.2 mg/m3	4372	090	MALE	EOE	79.9	40.8	23.6	0.3	6.6	4.7
3.2 mg/m3	4372	092	MALE	REC	83.1	50.5	21.8	0.2	6.4	5.1
3.2 mg/m3	4372	096	MALE	REC	70.0	40.9	23.3	0.2	5.7	4.2
3.2 mg/m3	4372	100	MALE	EOE	94.2	44.1	21.9	0.2	5.8	4.6
3.2 mg/m3	4372	111	MALE	REC	83.0	50.9	23.8	0.1	6.0	4.2
3.2 mg/m3	4372	112	MALE	REC	69.1	58.5	18.2	0.2	6.1	4.0

CONCENTRATION OF Cu-Zn	EXPT NUMBER	ANIMAL NUMBER	ANIMAL SEX	SACRIFICE CODE	ALKP	SGPT	BUN	TBIL	TPRO	ALB
3.2 mg/m3	4372	576	FEMALE	REC	87.7	38.2	25.6	0.2	5.7	4.6
3.2 mg/m3	4372	585	FEMALE	REC	69.6	43.7	22.7	0.3	6.3	4.7
3.2 mg/m3	4372	590	FEMALE	EOE	91.5	41.8	29.4	0.1	5.9	5.1
3.2 mg/m3	4372	598	FEMALE	REC	93.3	48.5	24.6	0.1	6.5	4.2
3.2 mg/m3	4372	599	FEMALE	EOE	89.5	34.2	28.5	0.1	6.6	4.8
3.2 mg/m3	4372	602	FEMALE	REC	73.3	40.1	22.3	0.2	6.2	5.2
3.2 mg/m3	4372	603	FEMALE	EOE	92.0	31.9	25.2	0.1	7.6	4.0
3.2 mg/m3	4372	606	FEMALE	REC	83.5	38.7	23.5	0.1	5.8	3.9
3.2 mg/m3	4372	608	FEMALE	EOE	80.3	47.1	25.9	0.1	5.8	5.2
3.2 mg/m3	4372	609	FEMALE	EOE	84.1	25.4	22.1	0.2	7.0	5.5
10 mg/m3	4373	122	MALE	REC	73.6	41.2	20.7	0.1	5.8	2.9
10 mg/m3	4373	127	MALE	REC	88.5	58.0	23.6	0.1	7.2	3.1
10 mg/m3	4373	128	MALE	EOE	98.0	33.9	21.0	0.0	6.9	4.6
10 mg/m3	4373	130	MALE	EOE	82.8	37.8	29.2	0.3	6.5	5.4
10 mg/m3	4373	134	MALE	REC	91.9	53.2	23.1	0.1	6.1	4.5
10 mg/m3	4373	135	MALE	REC	88.2	52.4	27.8	0.1	6.8	3.5
10 mg/m3	4373	136	MALE	EOE	73.0	40.9	27.2	0.3	7.2	5.9
10 mg/m3	4373	141	MALE	EOE	93.4	39.1	19.8	0.2	7.3	5.2
10 mg/m3	4373	142	MALE	EOE	83.4	40.9	25.2	0.1	6.8	5.4
10 mg/m3	4373	149	MALE	REC	63.4	49.8	23.0	0.2	5.7	4.4
10 mg/m3	4373	615	FEMALE	EOE	83.9	35.1	29.9	0.1	7.7	5.6
10 mg/m3	4373	616	FEMALE	REC	68.2	46.2	26.6	0.2	7.9	3.9
10 mg/m3	4373	627	FEMALE	REC	92.5	54.0	20.1	0.2	5.2	4.5
10 mg/m3	4373	628	FEMALE	EOE	91.5	40.8	27.2	0.0	7.3	5.1
10 mg/m3	4373	632	FEMALE	EOE	94.8	46.3	33.0	0.2	6.7	5.6
10 mg/m3	4373	633	FEMALE	EOE	93.8	36.7	27.4	0.1	7.1	4.6
10 mg/m3	4373	639	FEMALE	REC	63.0	37.9	23.9	0.2	5.7	1.9
10 mg/m3	4373	642	FEMALE	REC	71.6	40.2	18.6	0.0	6.4	3.3
10 mg/m3	4373	643	FEMALE	EOE	85.5	49.7	24.7	0.1	6.7	5.6
10 mg/m3	4373	650	FEMALE	REC	82.7	41.6	25.0	0.0	6.7	4.5

3. IMMUNOLOGY DATA FROM EVALUATIONS WITH LUNG-ASSOCIATED LYMPH NODES

CONCENTRATION OF Cu-Zn	EXPT. NUMBER	ANIMAL NUMBER	SEX	SAC CODE	TOTAL LYMPHOID CELLSx10^{-6}	ANTIBODY-FORMING CELLS PER MILLION LYMPHYCYTES	TOTAL ANTIBODY-FORMING CELLS
1.0 mg/m3	4371	042	M	REC	14.7	2235	32861
1.0 mg/m3	4371	045	M	EOE	6.6	315	2083
1.0 mg/m3	4371	053	M	EOE	7.6	1080	8208
1.0 mg/m3	4371	054	M	EOE	9.9	2925	28958
1.0 mg/m3	4371	058	M	EOE	6.9	812	5583
1.0 mg/m3	4371	065	M	REC	12.7	1203	15278
1.0 mg/m3	4371	073	M	REC	3.3	404	1333
1.0 mg/m3	4371	539	F	EOE	3.6	829	2958
1.0 mg/m3	4371	545	F	REC	10.6	13	139
1.0 mg/m3	4371	546	F	REC	9.0	763	6861
1.0 mg/m3	4371	561	F	EOE	10.6	1120	11875
1.0 mg/m3	4371	568	F	REC	6.1	824	5028
1.0 mg/m3	4371	574	F	EOE	12.3	474	5833
3.2 mg/m3	4372	077	M	EOE	19.9	663	13292
3.2 mg/m3	4372	078	M	REC	7.5	478	3583
3.2 mg/m3	4372	088	M	REC	6.8	1181	8028
3.2 mg/m3	4372	091	M	EOE	15.1	1325	20000
3.2 mg/m3	4372	094	M	EOE	21.8	835	18208
3.2 mg/m3	4372	097	M	EOE	25.7	1090	28000
3.2 mg/m3	4372	106	M	REC	7.2	31	222
3.2 mg/m3	4372	577	F	REC	8.3	238	1972
3.2 mg/m3	4372	583	F	REC	9.8	283	2778
3.2 mg/m3	4372	589	F	REC	4.3	116	500
3.2 mg/m3	4372	595	F	EOE	10.3	299	3083
3.2 mg/m3	4372	596	F	EOE	12.5	1210	15125
3.2 mg/m3	4372	597	F	EOE	6.2	785	4875
3.2 mg/m3	4372	610	F	REC	8.7	434	3778
10.0 mg/m3	4373	115	M	REC	11.1	10	111
10.0 mg/m3	4373	120	M	EOE	31.6	976	30833
10.0 mg/m3	4373	121	M	EOE	43.3	718	31083
10.0 mg/m3	4373	123	M	EOE	22.3	867	19333
10.0 mg/m3	4373	129	M	REC	9.8	241	2361
10.0 mg/m3	4373	131	M	REC	10.5	476	5000
10.0 mg/m3	4373	138	M	REC	9.8	828	8111
10.0 mg/m3	4373	619	F	REC	9.1	49	444
10.0 mg/m3	4373	621	F	EOE	18.8	758	14250
10.0 mg/m3	4373	622	F	REC	12.2	779	9500
10.0 mg/m3	4373	637	F	EOE	25.4	1453	36917
10.0 mg/m3	4373	641	F	EOE	17.1	950	16250
10.0 mg/m3	4373	645	F	REC	10.8	496	5361
10.0 mg/m3	4373	646	F	REC	7.4	71	528
10.0 mg/m3	4373	649	F	EOE	31.1	466	14500

CONCENTRATION OF Cu-Zn	EXPT. NUMBER	ANIMAL NUMBER	SEX	SAC CODE	TOTAL LYMPHOID CELLSx10 -6	ANTIBODY-FORMING CELLS PER MILLION LYMPHYCYTES	TOTAL ANTIBODY-FORMING CELLS
0 (SHAM)	4442	113	M	EOE	6.2	63	389
0 (SHAM)	4442	117	M	REC	13.3	357	4750
0 (SHAM)	4442	124	M	EOE	7.8	435	3389
0 (SHAM)	4442	125	M	REC	9.9	1395	13806
0 (SHAM)	4442	126	M	REC	7.6	826	6278
0 (SHAM)	4442	129	M	REC	11.2	2556	28625
0 (SHAM)	4442	133	M	EOE	9.3	287	2667
0 (SHAM)	4442	135	M	EOE	6.9	390	2692
0 (SHAM)	4442	514	F	REC	9.4	1333	12528
0 (SHAM)	4442	521	F	REC	9.6	822	7889
0 (SHAM)	4442	525	F	EOE	11.3	492	5556
0 (SHAM)	4442	528	F	REC	7.4	777	5750
0 (SHAM)	4442	529	F	EOE	11.9	896	10667
0 (SHAM)	4442	534	F	REC	11.6	826	9583
0 (SHAM)	4442	536	F	EOE	9.0	910	8194
0 (SHAM)	4442	537	F	EOE	7.8	662	5167
3.2 mg/m3	4444	169	M	EOE	6.2	67	417
3.2 mg/m3	4444	172	M	EOE	16.7	391	6528
3.2 mg/m3	4444	176	M	REC	10.3	833	8583
3.2 mg/m3	4444	178	M	EOE	17.3	300	5194
3.2 mg/m3	4444	183	M	REC	12.7	954	12111
3.2 mg/m3	4444	193	M	REC	3.6	85	306
3.2 mg/m3	4444	194	M	EOE	18.8	284	5333
3.2 mg/m3	4444	198	M	REC	7.4	188	1389
3.2 mg/m3	4444	571	F	EOE	18.0	315	5667
3.2 mg/m3	4444	572	F	REC	14.2	921	13083
3.2 mg/m3	4444	579	F	REC	7.4	556	4111
3.2 mg/m3	4444	584	F	REC	7.0	302	2111
3.2 mg/m3	4444	587	F	EOE	12.5	307	3833
3.2 mg/m3	4444	593	F	EOE	17.0	225	3833
3.2 mg/m3	4444	597	F	EOE	15.7	876	13750
3.2 mg/m3	4444	598	F	REC	5.7	107	611

4. PHAGOCYTOSIS AND BRONCHOPULMONARY LAVAGE FLUID CELL DIFFERENTIAL DATA

CONCENTRATION OF Cu-Zn	EXPT NUMBER	ANIMAL NUMBER	SEX	SACRIFICE CODE	NCELL	NEA	PPAM	PLYM	PPMN	PMAC	PEOS	NLYM	NPMN	NMAC	NEOS
1.0 mg/m3	4371	038	M	EOE	0.73	492	82	4.7	1.7	93.7	0	3.4	1.24	68.4	0
1.0 mg/m3	4371	043	M	EOE	0.82			1.7	2.3	96.0	0	1.4	1.89	78.7	0
1.0 mg/m3	4371	046	M	EOE	1.20	619	80	2.3	4.0	92.7	1.0	2.8	4.80	111.2	1.2
1.0 mg/m3	4371	048	M	REC	1.30			4.3	1.7	94.0	0	5.6	2.21	122.2	0
1.0 mg/m3	4371	050	M	REC	1.10	484	82	5.7	0	94.0	0.3	6.3	0	103.4	0.3
1.0 mg/m3	4371	051	M	REC	1.50	183	74	5.0	0	95.0	0	7.5	0	142.5	0
1.0 mg/m3	4371	052	M	EOE	1.00	399	75	9.0	12.3	77.7	1.0	9.0	12.30	77.7	1.0
1.0 mg/m3	4371	055	M	REC	1.00	308	77	15.7	0.7	83.7	0	15.7	0.70	83.7	0
1.0 mg/m3	4371	056	M	REC	1.10	312	62	13.7	1.3	85.0	0	15.1	1.43	93.5	0
1.0 mg/m3	4371	059	M	EOE	0.44	411	80	6.3	3.3	90.0	0.3	2.8	1.45	39.6	0.1
1.0 mg/m3	4371	060	M	REC	1.40	514	85	3.3	1.3	95.3	0	4.6	1.82	133.4	0
1.0 mg/m3	4371	061	M	EOE	1.00	470	79	8.0	2.0	88.7	1.3	8.0	2.00	88.7	1.3
1.0 mg/m3	4371	541	F	REC	0.63			9.3	0.7	89.7	0.3	5.9	0.44	56.5	0.2
1.0 mg/m3	4371	547	F	EOE	0.40	482	77	4.7	4.0	90.7	0.7	1.9	1.60	36.3	0.3
1.0 mg/m3	4371	548	F	EOE	0.54	355	74	8.7	3.3	86.7	1.3	4.7	1.78	46.8	0.7
1.0 mg/m3	4371	550	F	REC	1.30	312	71	9.0	0.7	90.3	0	11.7	0.91	117.4	0
1.0 mg/m3	4371	554	F	EOE	1.30	602	82	1.0	5.3	93.7	0	1.3	6.89	121.8	0
1.0 mg/m3	4371	555	F	REC	1.40	315	80	5.7	0	94.3	0	8.0	0	132.0	0
1.0 mg/m3	4371	560	F	REC	1.40	326	80	6.6	2.3	91.0	0	9.2	3.22	127.4	0
1.0 mg/m3	4371	562	F	REC	0.71	361	78	3.3	0.3	96.3	0	2.3	0.21	68.4	0
1.0 mg/m3	4371	563	F	REC	1.20	299	71	10.0	0	90.0	0	12.0	0	108.0	0
1.0 mg/m3	4371	564	F	EOE	0.99			3.3	0.7	96.0	0	3.3	0.69	95.0	0
1.0 mg/m3	4371	570	F	EOE	0.94	586	86	5.0	1.3	93.0	0.7	4.7	1.22	87.4	0.7
1.0 mg/m3	4371	571	F	EOE	1.20	396	90	13.3	1.7	85.0	0	16.0	2.04	102.0	0
3.2 mg/m3	4372	075	M	EOE	1.60	359	72	6.3	5.7	88.0	0	10.1	9.12	140.8	0
3.2 mg/m3	4372	081	M	EOE	1.40	249	76	10.0	3.7	85.7	0.7	14.0	5.18	120.0	1.0
3.2 mg/m3	4372	085	M	EOE	0.69	327	62	10.7	4.0	84.7	0.7	7.4	2.76	58.4	0.5
3.2 mg/m3	4372	086	M	REC	1.70	310	83	9.7	0.7	89.3	0.3	16.5	1.19	151.8	0.5
3.2 mg/m3	4372	087	M	EOE	2.60			10.3	1.3	88.0	0.3	26.8	3.38	228.8	0.8
3.2 mg/m3	4372	090	M	EOE	1.10	336	63	1.3	11.3	87.3	0	1.4	12.43	96.0	0
3.2 mg/m3	4372	092	M	REC	1.90	212	73	10.7	0.7	88.3	0.3	20.3	1.33	167.8	0.6
3.2 mg/m3	4372	093	M	REC	1.00			8.3	0	91.7	0	8.3	0	91.7	0
3.2 mg/m3	4372	096	M	REC	0.97	302	60	10.7	0.3	89.0	0	10.4	0.29	86.3	0
3.2 mg/m3	4372	100	M	EOE	2.20	381	72	1.0	4.3	93.0	1.7	2.2	9.46	204.6	3.7
3.2 mg/m3	4372	111	M	REC	1.50	507	79	8.3	0.3	91.3	0	12.5	0.45	137.0	0
3.2 mg/m3	4372	112	M	REC				19.0	0.3	80.3	0.3				

CONCENTRATION OF Cu-Zn	EXPT NUMBER	ANIMAL NUMBER	SEX	SACRIFICE CODE	NCELL	NEA	PPAM	PLYM	PPMN	PMAC	PEOS	NLYM	NPMN	NMAC	NEOS
3.2 mg/m3	4372	576	F	REC	0.85	285	69	4.0	0	96.0	0	3.4	0	81.6	0
3.2 mg/m3	4372	585	F	REC	0.77	141	69	16.0	0	84.0	0	12.3	0	64.7	0
3.2 mg/m3	4372	590	F	EOE	1.50	324	71	10.7	2.7	86.3	0.3	16.1	4.05	129.5	0.5
3.2 mg/m3	4372	593	F	EOE	1.20			8.3	5.0	86.3	0.3	10.0	6.00	103.6	0.4
3.2 mg/m3	4372	598	F	REC	1.70	133	62	19.9	1.2	78.8	0	33.8	2.04	134.0	0
3.2 mg/m3	4372	599	F	EOE	1.86	283	55	11.3	3.7	84.3	0.7	21.0	6.88	156.8	1.3
3.2 mg/m3	4372	602	F	REC	1.80	373	81	11.0	0.3	88.7	0	19.8	0.54	159.7	0
3.2 mg/m3	4372	603	F	EOE	0.94	366	60	11.0	4.7	83.3	1.0	10.3	4.42	78.3	0.9
3.2 mg/m3	4372	604	F	REC	0.60			10.7	3.0	86.0	0.3	6.4	1.80	51.6	0.2
3.2 mg/m3	4372	606	F	REC	1.10	339	80	16.0	0.3	83.3	0.3	17.6	0.33	91.6	0.3
3.2 mg/m3	4372	608	F	EOE	0.85	349	79	15.0	4.0	80.3	0.7	12.8	3.40	68.3	0.6
3.2 mg/m3	4372	609	F	EOE	1.33	333	63	14.7	3.3	82.0	0	19.6	4.39	109.1	0
10 mg/m3	4373	122	M	REC	1.10	246	63	18.0	1.0	81.0	0	19.8	1.10	89.1	0
10 mg/m3	4373	127	M	REC	0.73	271	75	9.3	0	90.4	0.3	6.8	0	66.0	0.2
10 mg/m3	4373	128	M	EOE	2.26	241	50	6.3	12.7	80.7	0.3	14.2	28.70	182.4	0.7
10 mg/m3	4373	130	M	FOE	4.50	246	75	13.3	3.7	81.3	1.7	59.9	16.65	365.9	7.7
10 mg/m3	4373	132	M	EOE	2.20			11.7	9.0	77.7	1.7	25.7	19.80	170.9	3.7
10 mg/m3	4373	134	M	REC	1.00	331	76	8.0	0	91.7	0.3	8.0	0	91.7	0.3
10 mg/m3	4373	135	M	REC	0.61	253	79	13.6	0.3	85.7	0	8.3	0.18	52.3	0
10 mg/m3	4373	136	M	EOE	2.80	228	71	4.0	7.7	87.7	0.7	11.2	21.56	245.6	2.0
10 mg/m3	4373	141	M	EOE	5.00	234	67	7.0	8.7	84.3	0	35.0	43.50	421.5	0
10 mg/m3	4373	142	M	EOE	2.38	194	47	8.7	18.0	73.0	0.3	20.7	42.84	173.7	0.7
10 mg/m3	4373	148	M	REC	1.30			8.3	2.0	89.7	0	10.8	2.60	116.6	0
10 mg/m3	4373	149	M	REC	1.90	296	69	7.7	0.3	92.0	0	14.6	0.57	174.8	0
10 mg/m3	4373	615	F	EOE	2.25	253	58	9.3	6.7	83.3	0.7	20.9	15.08	187.4	1.6
10 mg/m3	4373	616	F	REC	0.60	284	68	17.0	1.0	82.0	0	10.2	0.60	49.2	0
10 mg/m3	4373	625	F	EOE	2.50			9.0	3.3	87.7	0	22.5	8.25	219.3	0
10 mg/m3	4373	627	F	REC	0.82	303	76	20.9	0.3	78.7	0	17.1	0.25	64.5	0
10 mg/m3	4373	628	F	EOE	5.77	254	48	8.0	10.0	81.0	1.0	46.2	57.70	467.4	5.8
10 mg/m3	4373	631	F	REC	1.10			12.0	0	88.0	0	13.2	0	96.8	0
10 mg/m3	4373	632	F	EOE	3.30	334	71	14.0	11.7	74.3	0	46.2	38.61	245.1	0
10 mg/m3	4373	633	F	EOE	3.28	184	47	9.0	7.7	83.3	0.3	29.5	25.26	273.2	1.0
10 mg/m3	4373	639	F	REC	0.87	380	72	18.7	0.7	80.7	0	16.3	0.61	70.2	0
10 mg/m3	4373	642	F	REC	0.77	382	84	7.7	0	92.3	0	5.9	0	71.1	0
10 mg/m3	4373	643	F	EOE	1.50	343	68	15.3	6.3	77.7	0.7	23.0	9.45	116.6	1.1
10 mg/m3	4373	650	F	REC	0.48	246	70	10.7	4.0	82.0	3.3	5.1	1.92	39.4	1.6
0 (SHAM)	4442	109	M	REC	1.20	308	78	4.0	0.7	95.3	0	4.8	0.84	114.4	0
0 (SHAM)	4442	110	M	REC	1.40	537	93	4.3	2.3	93.3	0	6.0	3.22	130.6	0
0 (SHAM)	4442	112	M	EOE	1.10	307	69	10.0	0.5	89.6	0	11.0	0.55	98.6	0
0 (SHAM)	4442	114	M	REC	1.20	246	63	9.0	3.0	88.0	0	10.8	3.60	105.6	0
0 (SHAM)	4442	119	M	EOE	1.10	253	70	11.0	0.7	88.3	0	12.1	0.77	97.1	0

CONCENTRATION OF Cu-Zn	EXPT NUMBER	ANIMAL NUMBER	SEX	SACRIFICE CODE	NCELL	NEA	PPAM	PLYM	PPMN	PMAC	PEOS	NLYM	NPMN	NMAC	NEOS
0 (SHAM)	4442	122	M	EOE	0.83	316	75	5.0	0.7	94.3	0	4.2	0.58	78.3	0
0 (SHAM)	4442	127	M	EOE	1.10	357	80	7.3	0	92.7	0	8.0	0	102.0	0
0 (SHAM)	4442	128	M	EOE	1.10	313	69	9.0	0	91.0	0	9.9	0	100.1	0
0 (SHAM)	4442	130	M	REC	0.97	324	76	5.7	0	94.3	0	5.5	0	91.5	0
0 (SHAM)	4442	132	M	REC	1,00	445	85	5.7	1.7	92.7	0	5.7	1.70	92.7	0
0 (SHAM)	4442	136	M	EOE	1.40	360	81	9.7	0	90.3	0	13.6	0	126.4	0
0 (SHAM)	4442	137	M	REC	0.98	374	86	7.5	0	92.5	0	7.4	0	90.7	0
0 (SHAM)	4442	509	F	EOE	0.85	419	79	11.0	2.0	88.0	0	9.4	0.85	74.8	0
0 (SHAM)	4442	513	F	REC	0.77	383	80	3.7	0.7	95.7	0	2.8	0.54	73.7	0
0 (SHAM)	4442	518	F	REC	1.10	406	85	12.3	0.7	87.0	0	13.5	0.77	95.7	0
0 (SHAM)	4442	519	F	EOE	1.20	378	79	9.3	0.7	90.0	0	11.2	0.84	108.0	0
0 (SHAM)	4442	522	F	REC	1.10	489	86	11.3	2.0	86.7	0	12.4	2.20	95.4	0
0 (SHAM)	4442	523	F	REC	0.88	535	89	8.2	0.3	91.5	0	7.2	0.26	80.5	0
0 (SHAM)	4442	526	F	EOE	0.75	521	81	4.9	0	95.1	0	3.7	0	71.3	0
0 (SHAM)	4442	530	F	REC	0.93	325	70	3.3	0	96.7	0	3.1	0	89.9	0
0 (SHAM)	4442	531	F	EOE	0.65	384	74	3.0	0	97.0	0	2.0	0	63.1	0
0 (SHAM)	4442	533	F	EOE	1.50	377	72	28.0	1.0	71.0	0	42.0	1.50	106.5	0
0 (SHAM)	4442	535	F	REC	0.97	475	90	8.3	0.7	91.0	0	8.1	0.68	88.3	0
0 (SHAM)	4442	538	F	EOE	0.90	420	74	5.7	0.3	94.0	0	5.1	0.27	84.6	0
0.32 mg/m3	4443	140	M	REC	1.00	551	86	6.0	0.7	93.3	0	6.0	0.70	93.3	0
0.32 mg/m3	4443	142	M	REC	1.50	266	72	2.3	0.7	97.0	0	3.5	1.05	145.5	0
0.32 mg/m3	4443	145	M	EOE	0.90	351	77	4.0	0	96.0	0	3.6	0	86.4	0
0.32 mg/m3	4443	146	M	EOE	1.00	675	84	4.0	0.006	95.0	0	4.0	0.006	95.0	0
0.32 mg/m3	4443	147	M	REC	0.85	336	83	12.0	0.7	87.3	0	10.2	0.60	74.2	0
0.32 mg/m3	4443	148	M	EOE	0.96	472	73	8.3	1.0	90.7	0	8.0	0.96	87.1	0
0.32 mg/m3	4443	150	M	REC	0.99	227	71	5.0	0.3	94.7	0	5.0	0.30	93.8	0
0.32 mg/m3	4443	151	M	REC	1.30	477	90	10.7	0.7	88.7	0	13.9	0.91	115.3	0
0.32 mg/m3	4443	154	M	EOE	1.10	502	80	15.6	0	84.4	0	17.2	0	92.8	0
0.32 mg/m3	4443	156	M	EOE	0.94	475	75	3.3	0	96.7	0	3.1	0	90.9	0
0.32 mg/m3	4443	158	M	REC	0.79	401	83	11.0	0	88.7	0.3	8.7	0	70.1	0.2
0.32 mg/m3	4443	159	M	EOE	1.10	506	84	8.7	0.7	90.7	0	9.6	0.77	99.8	0
0.32 mg/m3	4443	541	F	REC	0.81	355	84	3.3	0.7	96.0	0	2.7	0.57	77.8	0
0.32 mg/m3	4443	542	F	EOE	0.96	604	84	8.0	0.003	92.0	0	7.7	0.003	88.3	0
0.32 mg/m3	4443	545	F	REC	0.88	526	87	4.7	0.3	95.0	0	4.1	0.26	83.6	0
0.32 mg/m3	4443	546	F	EOE	0.80	429	77	3.7	0.3	96.0	0	3.0	0.24	76.8	0
0.32 mg/m3	4443	547	F	EOE	0.80	488	82	4.6	1.3	94.0	0	3.7	1.04	75.2	0
0.32 mg/m3	4443	548	F	REC	0.87	361	82	4.0	0.3	95.7	0	3.5	0.26	83.3	0
0.32 mg/m3	4443	551	F	EOE	0.87	511	83	4.0	1.0	95.0	0	3.5	0.87	82.7	0
0.32 mg/m3	4443	552	F	REC	0.78	425	87	19.0	0	81.0	0	14.8	0	63.2	0
0.32 mg/m3	4443	555	F	EOE	0.97	378	75	7.3	0.3	92.4	0	7.1	0.29	89.6	0
0.32 mg/m3	4443	556	F	REC	0.87	270	68	7.0	2.3	90.7	0	6.1	2.001	78.9	0

CONCENTRATION OF Cu-Zn	EXPT NUMBER	ANIMAL NUMBER	SEX	SACRIFICE CODE	NCELL	NEA	PPAM	PLYM	PPMN	PMAC	PEOS	NLYM	NPMN	NMAC	NEOS
0.32 mg/m3	4443	557	F	REC	0.76	539	91	8.7	0.3	91.0	0	6.6	0.23	69.2	0
0.32 mg/m3	4443	560	F	EOE	0.91	485	85	13.3	0.3	86.3	0	12.1	0.27	78.5	0
3.2 mg/m3	4444	171	M	REC	0.86	336	88	9.7	0.3	90.0	0	8.3	0.26	77.4	0
3.2 mg/m3	4444	173	M	REC	0.89	396	88	9.3	0.7	90.0	0	8.3	0.62	80.1	0
3.2 mg/m3	4444	175	M	EOE	1.00	543	77	11.0	1.0	88.0	0	11.0	1.00	88.0	0
3.2 mg/m3	4444	180	M	EOE	1.10	472	81	7.0	0.003	93.0	0	7.7	0.0033	102.3	0
3.2 mg/m3	4444	182	M	EOE	1.20	472	75	10.3	2.0	87.7	0	12.4	2.40	105.2	0
3.2 mg/m3	4444	184	M	REC	0.85	361	83	10.6	0	89.4	0	9.0	0	76.0	0
3.2 mg/m3	4444	187	M	EOE	1.60	600	74	11.0	2.3	87.0	0	17.6	3.68	139.2	0
3.2 mg/m3	4444	188	M	REC	0.85	265	70	7.3	0.3	92.3	0	6.2	0.26	78.5	0
3.2 mg/m3	4444	190	M	EOE	2.00	413	85	16.3	0.7	83.1	0	32.6	1.40	166.2	0
3.2 mg/m3	4444	195	M	REC	1.00	235	72	6.3	0	93.7	0	6.3	0	93.7	0
3.2 mg/m3	4444	196	M	REC	1.30	478	89	8.0	0.3	91.7	0	10.4	0.39	119.2	0
3.2 mg/m3	4444	197	M	EOE	1.40	457	75	12.0	7.0	80.0	0	16.8	9.80	112.0	0
3.2 mg/m3	4444	569	F	REC	0.73	523	89	5.0	0	95.0	0	3.7	0	69.4	0
3.2 mg/m3	4444	574	F	EOE	0.99	356	76	7.0	3.7	89.3	0	6.9	3.66	88.4	0
3.2 mg/m3	4444	576	F	REC	0.84	622	92	6.7	0	93.3	0	5.6	0	78.4	0
3.2 mg/m3	4444	577	F	REC	0.62	486	96	7.0	1.0	92.0	0	4.3	0.62	57.0	0
3.2 mg/m3	4444	578	F	EOE	1.30	645	80	10.0	2.0	88.0	0	13.0	2.60	114.4	0
3.2 mg/m3	4444	580	F	REC	1.10	452	83	11.0	1.0	88.0	0	12.1	1.10	96.8	0
3.2 mg/m3	4444	581	F	EOE	0.92	386	63	10.7	1.0	87.0	1.3	9.8	0.92	80.0	1.2
3.2 mg/m3	4444	582	F	REC	0.84	420	91	10.0	0	90.0	0	8.4	0	75.6	0
3.2 mg/m3	4444	583	F	EOE	1.60	471	81	5.6	3.3	91.0	0	9.0	5.28	145.6	0
3.2 mg/m3	4444	585	F	REC	0.85	425	86	7.0	0.3	92.7	0	6.0	0.26	78.8	0
3.2 mg/m3	4444	586	F	EOE	1.30	365	88	14.0	0.3	85.7	0	18.2	0.39	111.4	0
3.2 mg/m3	4444	590	F	EOE	0.73	419	64	11.0	1.0	88.0	0	8.0	0.73	64.2	0

5. BRONCHOALVEOLAR LAVAGE FLUID BIOCHEMISTRY DATA

CONCENTRATION OF Cu-Zn	EXPT. NUMBER	ANIMAL NUMBER	ANIMAL SEX	SAC CODE	BGLUL	ALKPL	LDHL	TPROL
1.0 mg/m3	4371	038	M	EOE	0.38	372	973	1.67
1.0 mg/m3	4371	043	M	EOE	1.76	502	1588	1.70
1.0 mg/m3	4371	046	M	EOE	1.26	568	1648	1.70
1.0 mg/m3	4371	048	M	REC	1.51	323	796	1.10
1.0 mg/m3	4371	050	M	REC	1.26	392	828	1.20
1.0 mg/m3	4371	051	M	REC	2.27	432	741	1.69
1.0 mg/m3	4371	052	M	EOE	0.89	57	785	2.01
1.0 mg/m3	4371	055	M	REC	2.39	283	84	0.07
1.0 mg/m3	4371	056	M	REC	4.79	888	2926	2.26
1.0 mg/m3	4371	059	M	EOE	1.13	427	747	1.15
1.0 mg/m3	4371	060	M	REC	2.52	349	1172	2.59
1.0 mg/m3	4371	061	M	EOE	2.02	515	774	1.85
1.0 mg/m3	4371	541	F	REC	1.21	225	587	0.62
1.0 mg/m3	4371	547	F	EOE	1.11	457	1474	1.67
1.0 mg/m3	4371	548	F	EOE	2.82	604	2550	1.67
1.0 mg/m3	4371	550	F	REC	1.71	306	507	1.07
1.0 mg/m3	4371	554	F	EOE	1.31	365	585	1.72
1.0 mg/m3	4371	555	F	REC	1.51	288	281	0.80
1.0 mg/m3	4371	560	F	REC	1.21	246	231	0.50
1.0 mg/m3	4371	562	F	REC	1.11	327	836	1.03
1.0 mg/m3	4371	563	F	REC	0.81	256	529	0.99
1.0 mg/m3	4371	564	F	EOE	1.11	320	494	0.95
1.0 mg/m3	4371	570	F	EOE	1.62	430	1562	1.81
1.0 mg/m3	4371	571	F	EOE	1.62	310	314	1.95

CONCENTRATION OF Cu-Zn	EXPT. NUMBER	ANIMAL NUMBER	ANIMAL SEX	SAC CODE	BGLUL	ALKPL	LDHL	TPROL
3.2 mg/m3	4372	075	M	EOE	1.26	543	1931	2.39
3.2 mg/m3	4372	081	M	EOE	2.78	687	1799	1.85
3.2 mg/m3	4372	085	M	EOE	0.89	363	718	1.91
3.2 mg/m3	4372	086	M	REC	2.65	346	761	1.14
3.2 mg/m3	4372	087	M	EOE	3.28	489	1563	2.30
3.2 mg/m3	4372	090	M	EOE	2.02	354	1163	2.37
3.2 mg/m3	4372	092	M	REC	2.90	269	767	0.75
3.2 mg/m3	4372	093	M	REC	1.26	260	687	1.02
3.2 mg/m3	4372	096	M	REC	2.14	378	966	0.41
3.2 mg/m3	4372	100	M	EOE	1.52	693	2598	1.77
3.2 mg/m3	4372	111	M	REC	1.51	347	480	1.60
3.2 mg/m3	4372	112	M	REC	1.63	282	581	1.26
3.2 mg/m3	4372	576	F	REC	1.41	263	430	0.94
3.2 mg/m3	4372	585	F	REC	0.81	365	793	1.14
3.2 mg/m3	4372	590	F	EOE	1.01	531	2479	1.70
3.2 mg/m3	4372	598	F	REC	3.53	330	1812	2.10
3.2 mg/m3	4372	599	F	EOE	1.71	342	1323	1.48
3.2 mg/m3	4372	602	F	REC	2.02	296	1802	1.01
3.2 mg/m3	4372	603	F	EOE	1.91	390	1693	1.52
3.2 mg/m3	4372	604	F	REC	0.70	196	192	0.23
3.2 mg/m3	4372	606	F	REC	0.90	188	652	0.86
3.2 mg/m3	4372	608	F	EOE	1.31	363	1354	1.65
3.2 mg/m3	4372	609	F	EOE	2.52	401	1621	1.63

CONCENTRATION OF Cu-Zn	EXPT. NUMBER	ANIMAL NUMBER	ANIMAL SEX	SAC CODE	BGLUL	ALKPL	LDHL	TPROL
10 mg/m3	4373	122	M	REC	2.01	286	794	0.78
10 mg/m3	4373	127	M	REC	0	625	1780	2.25
10 mg/m3	4373	128	M	EOE	12.98	353	2215	2.87
10 mg/m3	4373	130	M	EOE	6.30	285	1541	3.51
10 mg/m3	4373	132	M	EOE	5.42	235	1039	2.65
10 mg/m3	4373	134	M	REC	0.50	220	900	1.40
10 mg/m3	4373	135	M	REC	0.76	390	971	1.47
10 mg/m3	4373	136	M	EOE	8.57	687	3048	2.91
10 mg/m3	4373	141	M	EOE	7.31	374	1814	3.01
10 mg/m3	4373	142	M	EOE	10.58	449	3721	4.06
10 mg/m3	4373	148	M	REC	3.02	253	591	0.75
10 mg/m3	4373	149	M	REC	2.01	205	476	0.94
10 mg/m3	4373	615	F	EOE	2.52	262	1802	2.64
10 mg/m3	4373	616	F	REC	1.91	210	978	2.02
10 mg/m3	4373	625	F	EOE	2.62	231	934	1.93
10 mg/m3	4373	627	F	REC	0.30	170	498	0.56
10 mg/m3	4373	628	F	EOE	12.20	298	2811	3.22
10 mg/m3	4373	631	F	REC	1.21	226	718	1.07
10 mg/m3	4373	632	F	EOE	3.73	262	940	2.07
10 mg/m3	4373	633	F	EOE	10.28	373	3892	3.35
10 mg/m3	4373	639	F	REC	2.52	262	710	1.02
10 mg/m3	4373	642	F	REC	0.50	282	700	1.45
10 mg/m3	4373	643	F	EOE	2.42	221	813	1.62
10 mg/m3	4373	650	F	REC	1.62	214	949	0.77

CONCENTRATION OF Cu-Zn	EXPT. NUMBER	ANIMAL NUMBER	ANIMAL SEX	SAC CODE	BGLUL	ALKPL	LDHL	TPROL
0 (SHAM)	4442	109	M	REC	1.26	339	566	0.98
0 (SHAM)	4442	110	M	REC	1.51	280	486	1.95
0 (SHAM)	4442	112	M	EOE	0.50	304	389	1.90
0 (SHAM)	4442	114	M	REC	1.26	290	458	1.62
0 (SHAM)	4442	119	M	EOE	1.64	392	451	1.86
0 (SHAM)	4442	122	M	EOE	1.64	300	324	1.68
0 (SHAM)	4442	127	M	EOE	1.76	394	456	1.62
0 (SHAM)	4442	128	M	EOE	1.13	307	189	1.96
0 (SHAM)	4442	130	M	REC	0.50	391	537	1.64
0 (SHAM)	4442	132	M	REC	1.26	290	389	1.83
0 (SHAM)	4442	136	M	EOE	1.26	363	383	1.75
0 (SHAM)	4442	137	M	REC	1.01	359	327	2.57
0 (SHAM)	4442	509	F	EOE	1.21	106	452	1.43
0 (SHAM)	4442	513	F	REC	0.90	204	434	0.94
0 (SHAM)	4442	518	F	REC	2.02	302	489	1.98
0 (SHAM)	4442	519	F	EOE	1.31	250	412	1.42
0 (SHAM)	4442	522	F	REC	0.70	206	358	1.34
0 (SHAM)	4442	523	F	REC	1.31	194	385	1.13
0 (SHAM)	4442	526	F	EOE	0.61	240	283	1.52
0 (SHAM)	4442	530	F	REC	0.50	150	491	0.86
0 (SHAM)	4442	531	F	EOE	1.21	271	230	1.06
0 (SHAM)	4442	533	F	EOE	2.22	248	588	1.02
0 (SHAM)	4442	535	F	REC	1.31	219	431	1.51
0 (SHAM)	4442	538	F	EOE	0.70	242	463	1.36

CONCENTRATION OF Cu-Zn	EXPT. NUMBER	ANIMAL NUMBER	ANIMAL SEX	SAC CODE	BGLUL	ALKPL	LDHL	TPROL
0.32 mg/m3	4443	140	M	REC	1.01	310	483	1.44
0.32 mg/m3	4443	142	M	REC	0.88	440	835	2.47
0.32 mg/m3	4443	145	M	EOE	1.13	481	377	1.80
0.32 mg/m3	4443	146	M	EOE	3.53	323	480	1.40
0.32 mg/m3	4443	147	M	REC	1.63	256	308	1.99
0.32 mg/m3	4443	148	M	EOE	1.51	396	476	1.30
0.32 mg/m3	4443	150	M	REC	1.64	257	420	0.28
0.32 mg/m3	4443	151	M	REC	1.89	364	546	1.88
0.32 mg/m3	4443	154	M	EOE	1.13	273	413	1.39
0.32 mg/m3	4443	156	M	EOE	2.02	426	554	1.86
0.32 mg/m3	4443	158	M	REC	2.26	389	543	2.52
0.32 mg/m3	4443	159	M	EOE	1.13	221	280	1.14
0.32 mg/m3	4443	541	F	REC	0.70	183	514	0.74
0.32 mg/m3	4443	542	F	EOE	1.01	274	301	0.87
0.32 mg/m3	4443	545	F	REC	0.80	231	374	1.92
0.32 mg/m3	4443	546	F	EOE	1.21	288	338	1.19
0.32 mg/m3	4443	547	F	EOE	1.01	320	407	1.57
0.32 mg/m3	4443	548	F	REC	1.61	302	459	1.98
0.32 mg/m3	4443	551	F	EOE	1.91	308	267	0.93
0.32 mg/m3	4443	552	F	REC	1.31	215	496	1.22
0.32 mg/m3	4443	555	F	EOE	3.22	291	324	1.10
0.32 mg/m3	4443	556	F	REC	0.90	198	375	0.64
0.32 mg/m3	4443	557	F	REC	0.40	262	505	0.99
0.32 mg/m3	4443	560	F	EOE	0.61	256	450	1.07

CONCENTRATION OF Cu-Zn	EXPT. NUMBER	ANIMAL NUMBER	ANIMAL SEX	SAC CODE	BGLUL	ALKPL	LDHL	TPROL
3.2 mg/m3	4444	171	M	REC	1.76	244	389	1.90
3.2 mg/m3	4444	173	M	REC	1.51	237	502	1.56
3.2 mg/m3	4444	175	M	EOE	1.64	366	705	1.76
3.2 mg/m3	4444	180	M	EOE	1.76	410	506	1.32
3.2 mg/m3	4444	182	M	EOE	1.01	175	795	1.32
3.2 mg/m3	4444	184	M	REC	0.63	258	438	1.30
3.2 mg/m3	4444	187	M	EOE	1.26	388	501	2.11
3.2 mg/m3	4444	188	M	REC	0.63	217	269	0.95
3.2 mg/m3	4444	190	M	EOE	0.38	683	702	1.77
3.2 mg/m3	4444	195	M	REC	1.13	261	559	1.45
3.2 mg/m3	4444	196	M	REC	1.39	341	577	2.08
3.2 mg/m3	4444	197	M	EOE	0.88	507	489	2.00
3.2 mg/m3	4444	569	F	REC	1.41	191	461	1.10
3.2 mg/m3	4444	574	F	EOE	1.21	328	526	1.13
3.2 mg/m3	4444	576	F	REC	1.06	163	374	0.81
3.2 mg/m3	4444	577	F	REC	0.80	150	298	1.17
3.2 mg/m3	4444	578	F	EOE	1.41	378	346	1.06
3.2 mg/m3	4444	580	F	REC	1.61	118	346	1.27
3.2 mg/m3	4444	581	F	EOE	1.11	303	255	1.24
3.2 mg/m3	4444	582	F	REC	0.40	194	286	1.29
3.2 mg/m3	4444	583	F	EOE	3.42	508	966	2.29
3.2 mg/m3	4444	585	F	REC	1.01	202	371	1.15
3.2 mg/m3	4444	586	F	EOE	1.62	362	769	1.36
3.2 mg/m3	4444	590	F	EOE	1.01	240	295	1.09

6. DATA FOR BRONCHOALVEOLAR LAVAGE FLUID CONTENT OF COLLAGEN

					COLLAGEN IN LUNG PER:	
CONCENTRATION of Cu-Zn	EXPT NUMBER	ANIMAL NUMBER	ANIMAL SEX	SACRIFICE CODE	GRAM CONTROL LUNG (ug/g)	kg BODY WT (ug/kg)
1.0 mg/m3	4371	038	MALE	EOE	38.84	169.5
1.0 mg/m3	4371	043	MALE	EOE	63.77	289.9
1.0 mg/m3	4371	046	MALE	EOE	55.44	241.1
1.0 mg/m3	4371	052	MALE	EOE	39.22	188.4
1.0 mg/m3	4371	059	MALE	EOE	45.33	224.4
1.0 mg/m3	4371	061	MALE	EOE	47.96	217.5
1.0 mg/m3	4371	547	FEMALE	EOE	102.88	529.1
1.0 mg/m3	4371	548	FEMALE	EOE	75.52	409.7
1.0 mg/m3	4371	554	FEMALE	EOE	87.88	378.3
1.0 mg/m3	4371	564	FEMALE	EOE	49.96	262.7
1.0 mg/m3	4371	570	FEMALE	EOE	80.85	451.2
1.0 mg/m3	4371	571	FEMALE	EOE	74.92	399.2
1.0 mg/m3	4371	048	MALE	REC	107.84	456.3
1.0 mg/m3	4371	050	MALE	REC	65.68	250.0
1.0 mg/m3	4371	051	MALE	REC	70.04	280.7
1.0 mg/m3	4371	055	MALE	REC	37.62	155.4
1.0 mg/m3	4371	056	MALE	REC	83.11	329.2
1.0 mg/m3	4371	060	MALE	REC	75.68	284.8
1.0 mg/m3	4371	541	FEMALE	REC	41.89	217.4
1.0 mg/m3	4371	550	FEMALE	REC	36.09	18C.8
1.0 mg/m3	4371	555	FEMALE	REC	61.25	307.7
1.0 mg/m3	4371	560	FEMALE	REC	62.02	301.6
1.0 mg/m3	4371	562	FEMALE	REC	68.26	367.2
1.0 mg/m3	4371	563	FEMALE	REC	107.04	544.3

					COLLAGEN IN LUNG PER:	
CONCENTRATION of Cu-Zn	EXPT NUMBER	ANIMAL NUMBER	ANIMAL SEX	SACRIFICE CODE	GRAM CONTROL LUNG (ug/g)	kg BODY WT (ug/kg)
3.2 mg/m3	4372	075	MALE	EOE	43.11	190.3
3.2 mg/m3	4372	081	MALE	EOE	70.73	319.3
3.2 mg/m3	4372	085	MALE	EOE	41.00	185.3
3.2 mg/m3	4372	087	MALE	EOE	53.93	230.8
3.2 mg/m3	4372	090	MALE	EOE	53.60	235.5
3.2 mg/m3	4372	100	MALE	EOE	71.34	312.4
3.2 mg/m3	4372	590	FEMALE	EOE	57.34	297.3
3.2 mg/m3	4372	599	FEMALE	EOE	75.58	394.1
3.2 mg/m3	4372	603	FEMALE	EOE	66.74	353.4
3.2 mg/m3	4372	608	FEMALE	EOE	43.94	237.7
3.2 mg/m3	4372	609	FEMALE	EOE	80.32	414.8
3.2 mg/m3	4372	086	MALE	REC	58.08	227.3
3.2 mg/m3	4372	092	MALE	REC	74.34	263.3
3.2 mg/m3	4372	093	MALE	REC	82.53	322.1
3.2 mg/m3	4372	096	MALE	REC	72.75	285.5
3.2 mg/m3	4372	111	MALE	REC	68.49	268.0
3.2 mg/m3	4372	112	MALE	REC	49.65	189.8
3.2 mg/m3	4372	576	FEMALE	REC	51.79	263.3
3.2 mg/m3	4372	585	FEMALE	REC	49.21	232.0
3.2 mg/m3	4372	598	FEMALE	REC	63.05	298.6
3.2 mg/m3	4372	602	FEMALE	REC	84.96	439.2
3.2 mg/m3	4372	604	FEMALE	REC	52.54	278.4
3.2 mg/m3	4372	606	FEMALE	REC	61.99	309.8

CONCENTRATION of Cu-Zn	EXPT NUMBER	ANIMAL NUMBER	ANIMAL SEX	SACRIFICE CODE	COLLAGEN IN LUNG PER: GRAM CONTROL LUNG (ug/g)	COLLAGEN IN LUNG PER: kg BODY WT (ug/kg)
10 mg/m3	4373	128	MALE	EOE	83.33	386.7
10 mg/m3	4373	130	MALE	EOE	61.28	294.3
10 mg/m3	4373	132	MALE	EOE	78.30	391.3
10 mg/m3	4373	136	MALE	EOE	68.61	331.2
10 mg/m3	4373	141	MALE	EOE	104.14	472.3
10 mg/m3	4373	142	MALE	EOE	76.01	352.9
10 mg/m3	4373	615	FEMALE	EOE	102.16	559.5
10 mg/m3	4373	625	FEMALE	EOE	74.56	388.8
10 mg/m3	4373	628	FEMALE	EOE	135.90	776.5
10 mg/m3	4373	632	FEMALE	EOE	79.03	440.1
10 mg/m3	4373	633	FEMALE	EOE	90.04	504.9
10 mg/m3	4373	643	FEMALE	EOE	59.95	341.8
10 mg/m3	4373	122	MALE	REC	50.08	179.9
10 mg/m3	4373	127	MALE	REC	67.35	270.2
10 mg/m3	4373	134	MALE	REC	52.85	204.0
10 mg/m3	4373	135	MALE	REC	63.78	254.7
10 mg/m3	4373	148	MALE	REC	55.63	218.8
10 mg/m3	4373	149	MALE	REC	32.07	128.7
10 mg/m3	4373	616	FEMALE	REC	55.77	283.7
10 mg/m3	4373	627	FEMALE	REC	59.66	308.7
10 mg/m3	4373	631	FEMALE	REC	69.00	356.6
10 mg/m3	4373	639	FEMALE	REC	69.32	351.4
10 mg/m3	4373	642	FEMALE	REC	54.77	306.9
10 mg/m3	4373	650	FEMALE	REC	58.68	311.1

					COLLAGEN IN LUNG PER:	
CONCENTRATION of Cu-Zn	EXPT NUMBER	ANIMAL NUMBER	ANIMAL SEX	SACRIFICE CODE	GRAM CONTROL LUNG (ug/g)	kg BODY WT (ug/kg)
0 (SHAM)	4442	112	MALE	EOE	38.78	165.8
0 (SHAM)	4442	119	MALE	EOE	44.39	195.5
0 (SHAM)	4442	122	MALE	EOE	34.84	146.6
0 (SHAM)	4442	127	MALE	EOE	42.19	176.6
0 (SHAM)	4442	128	MALE	EOE	30.24	130.1
0 (SHAM)	4442	136	MALE	EOE	44.31	183.7
0 (SHAM)	4442	509	FEMALE	EOE	43.69	225.3
0 (SHAM)	4442	519	FEMALE	EOE	59.39	297.0
0 (SHAM)	4442	526	FEMALE	EOE	65.85	349.3
0 (SHAM)	4442	531	FEMALE	EOE	51.72	257.7
0 (SHAM)	4442	533	FEMALE	EOE	45.49	238.5
0 (SHAM)	4442	538	FEMALE	EOE	44.17	230.7
0 (SHAM)	4442	109	MALE	REC	39.28	133.5
0 (SHAM)	4442	110	MALE	REC	38.21	132.7
0 (SHAM)	4442	114	MALE	REC	41.70	148.9
0 (SHAM)	4442	130	MALE	REC	40.51	136.2
0 (SHAM)	4442	132	MALE	REC	36.46	120.4
0 (SHAM)	4442	137	MALE	REC	43.84	151.1
0 (SHAM)	4442	513	FEMALE	REC	38.24	175.1
0 (SHAM)	4442	518	FEMALE	REC	57.48	259.7
0 (SHAM)	4442	522	FEMALE	REC	40.18	191.5
0 (SHAM)	4442	523	FEMALE	REC	50.38	238.6
0 (SHAM)	4442	530	FEMALE	REC	87.18	423.9
0 (SHAM)	4442	535	FEMALE	REC	57.93	272.7

CONCENTRATION of Cu-Zn	EXPT NUMBER	ANIMAL NUMBER	ANIMAL SEX	SACRIFICE CODE	COLLAGEN IN LUNG PER: GRAM CONTROL LUNG (ug/g)	kg BODY WT (ug/kg)
0.32 mg/m3	4443	145	MALE	EOE	56.46	243.1
0.32 mg/m3	4443	146	MALE	EOE	52.88	221.3
0.32 mg/m3	4443	148	MALE	EOE	42.18	177.0
0.32 mg/m3	4443	154	MALE	EOE	42.96	187.4
0.32 mg/m3	4443	156	MALE	EOE	52.36	217.4
0.32 mg/m3	4443	159	MALE	EOE	32.99	142.5
0.32 mg/m3	4443	542	FEMALE	EOE	46.64	224.7
0.32 mg/m3	4443	546	FEMALE	EOE	54.62	283.0
0.32 mg/m3	4443	547	FEMALE	EOE	61.36	333.6
0.32 mg/m3	4443	551	FEMALE	EOE	40.60	194.9
0.32 mg/m3	4443	555	FEMALE	EOE	48.50	252.1
0.32 mg/m3	4443	560	FEMALE	EOE	51.64	276.1
0.32 mg/m3	4443	140	MALE	REC	51.52	183.0
0.32 mg/m3	4443	142	MALE	REC	75.72	260.6
0.32 mg/m3	4443	147	MALE	REC	51.65	180.6
0.32 mg/m3	4443	150	MALE	REC	40.09	157.3
0.32 mg/m3	4443	151	MALE	REC	43.74	153.9
0.32 mg/m3	4443	158	MALE	REC	163.19	583.7
0.32 mg/m3	4443	541	FEMALE	REC	54.06	277.3
0.32 mg m3	4443	545	FEMALE	REC	51.00	225.8
0.32 mg/m3	4443	548	FEMALE	REC	66.80	301.0
0.32 mg/m3	4443	552	FEMALE	REC	44.35	211.8
0.32 mg/m3	4443	556	FEMALE	REC	48.06	236.5
0.32 mg/m3	4443	557	FEMALE	REC	46.96	221.9

CONCENTRATION of Cu-Zn	EXPT NUMBER	ANIMAL NUMBER	ANIMAL SEX	SACRIFICE CODE	COLLAGEN IN LUNG PER: GRAM CONTROL LUNG (ug/g)	COLLAGEN IN LUNG PER: kg BODY WT (ug/kg)
3.2 mg/m3	4444	175	MALE	EOE	41.67	171.3
3.2 mg/m3	4444	180	MALE	EOE	48.10	209.1
3.2 mg/m3	4444	187	MALE	EOE	50.66	214.4
3.2 mg/m3	4444	190	MALE	EOE	49.57	216.3
3.2 mg/m3	4444	197	MALE	EOE	42.32	181.0
3.2 mg/m3	4444	574	FEMALE	EOE	64.22	327.8
3.2 mg/m3	4444	578	FEMALE	EOE	56.27	300.5
3.2 mg/m3	4444	581	FEMALE	EOE	57.68	298.7
3.2 mg/m3	4444	583	FEMALE	EOE	70.80	361.6
3.2 mg/m3	4444	586	FEMALE	EOE	88.99	446.4
3.2 mg/m3	4444	590	FEMALE	EOE	36.06	181.6
3.2 mg/m3	4444	171	MALE	REC	35.22	137.1
3.2 mg/m3	4444	173	MALE	REC	46.64	165.0
3.2 mg/m3	4444	184	MALE	REC	32.69	118.7
3.2 mg/m3	4444	188	MALE	REC	46.36	167.6
3.2 mg/m3	4444	195	MALE	REC	50.15	176.9
3.2 mg/m3	4444	196	MALE	REC	43.10	150.7
3.2 mg/m3	4444	569	FEMALE	REC	43.13	202.1
3.2 mg/m3	4444	576	FEMALE	REC	42.77	204.8
3.2 mg/m3	4444	577	FEMALE	REC	45.99	218.7
3.2 mg/m3	4444	580	FEMALE	REC	62.96	301.0
3.2 mg/m3	4444	582	FEMALE	REC	40.35	187.7
3.2 mg/m3	4444	585	FEMALE	REC	49.20	234.5

7. DATA FOR TOTAL COLLAGEN CONTENT OF LUNG

CONCENTRATION of Cu-Zn	EXPT NUMBER	ANIMAL NUMBER	ANIMAL SEX	SACRIFICE CODE	BODY WEIGHT IN GRAMS	LUNG WEIGHT IN GRAMS	TOTAL LUNG COLLAGEN mg/g CONTROL LUNG	TOTAL LUNG COLLAGEN mg/kg BODY WEIGHT
3.2 mg/m3	4372	075	MALE	EOE	320.6	1.90	17.20	75.91
3.2 mg/m3	4372	081	MALE	EOE	313.5	1.60	20.97	94.64
3.2 mg/m3	4372	085	MALE	EOE	313.0	1.29	18.58	83.98
3.2 mg/m3	4372	090	MALE	EOE	322.1	1.37	17.03	74.82
3.2 mg/m3	4372	100	MALE	EOE	323.1	1.47	19.49	85.38
3.2 mg/m3	4372	590	FEMALE	EOE	192.8	1.05	16.95	87.92
3.2 mg/m3	4372	599	FEMALE	EOE	191.8	1.19	19.84	103.47
3.2 mg/m3	4372	603	FEMALE	EOE	188.9	1.08	18.34	97.11
3.2 mg/m3	4372	608	FEMALE	EOE	184.9	0.88	16.23	87.81
3.2 mg/m3	4372	609	FEMALE	EOE	193.7	1.05	16.35	84.41
10 mg/m3	4373	122	MALE	REC	360.1	1.52	17.52	62.97
10 mg/m3	4373	127	MALE	REC	322.6	1.39	12.81	51.39
10 mg/m3	4373	128	MALE	EOE	304.9	1.86	19.74	91.63
10 mg/m3	4373	130	MALE	EOE	294.7	1.59	16.13	77.44
10 mg/m3	4373	134	MALE	REC	335.2	1.67	22.09	85.29
10 mg/m3	4373	135	MALE	REC	324.1	1.30	15.26	60.94
10 mg/m3	4373	136	MALE	EOE	293.1	1.41	19.14	92.42
10 mg/m3	4373	141	MALE	EOE	312.0	1.73	20.91	94.81
10 mg/m3	4373	142	MALE	EOE	304.8	1.82	17.95	83.32
10 mg/m3	4373	149	MALE	REC	322.4	1.36	20.91	83.93
10 mg/m3	4373	615	FEMALE	EOE	182.6	1.25	21.47	117.60
10 mg/m3	4373	616	FEMALE	REC	192.1	0.93	18.19	92.51
10 mg/m3	4373	627	FEMALE	REC	188.8	1.15	12.04	62.32
10 mg/m3	4373	628	FEMALE	EOE	175.0	1.31	21.96	125.46

CONCENTRATION of Cu-Zn	EXPT NUMBER	ANIMAL NUMBER	ANIMAL SEX	SACRIFICE CODE	BODY WEIGHT IN GRAMS	LUNG WEIGHT IN GRAMS	TOTAL LUNG COLLAGEN mg/g CONTROL LUNG	TOTAL LUNG COLLAGEN mg/kg BODY WEIGHT
10 mg/m3	4373	632	FEMALE	EOE	179.6	0.72	13.23	73.57
10 mg/m3	4373	633	FEMALE	EOE	178.3	1.24	20.07	112.53
10 mg/m3	4373	639	FEMALE	REC	192.7	0.90	19.10	96.81
10 mg/m3	4373	642	FEMALE	REC	174.3	0.89	15.62	87.55
10 mg/m3	4373	643	FEMALE	EOE	175.4	1.09	18.23	103.96
10 mg/m3	4373	650	FEMALE	REC	184.3	1.16	21.56	114.33
0 (SHAM)	4442	110	MALE	REC	372.5	1.24	16.62	57.73
0 (SHAM)	4442	119	MALE	EOE	321.2	1.29	14.12	62.21
0 (SHAM)	4442	128	MALE	EOE	328.9	1.43	15.38	66.18
0 (SHAM)	4442	132	MALE	REC	392.0	1.35	19.80	65.37
0 (SHAM)	4442	136	MALE	EOE	341.3	1.24	17.67	73.23
0 (SHAM)	4442	137	MALE	REC	375.4	1.20	11.83	40.78
0 (SHAM)	4442	519	FEMALE	EOE	200.0	1.21	21.52	107.59
0 (SHAM)	4442	522	FEMALE	REC	205.0	0.94	17.78	84.75
0 (SHAM)	4442	523	FEMALE	REC	206.3	0.87	18.47	87.46
0 (SHAM)	4442	533	FEMALE	EOE	190.7	0.89	15.12	79.28
0 (SHAM)	4442	535	FEMALE	REC	207.6	0.98	20.79	97.86
0 (SHAM)	4442	538	FEMALE	EOE	191.4	0.97	19.29	100.77
3.2 mg/m3	4444	175	MALE	EOE	344.2	1.49	16.55	68.03
3.2 mg/m3	4444	180	MALE	EOE	325.5	1.62	26.42	114.87
3.2 mg/m3	4444	182	MALE	EOE	323.8	1.54	18.10	79.09
3.2 mg/m3	4444	187	MALE	EOE	334.3	1.35	18.96	80.26
3.2 mg/m3	4444	190	MALE	EOE	324.3	1.29	16.31	71.17
3.2 mg/m3	4444	574	FEMALE	EOE	195.9	1.05	21.00	107.17
3.2 mg/m3	4444	581	FEMALE	EOE	193.1	1.19	20.43	105.79
3.2 mg/m3	4444	583	FEMALE	EOE	195.8	0.98	20.59	105.20
3.2 mg/m3	4444	586	FEMALE	EOE	199.4	1.00	18.64	93.51
3.2 mg/m3	4444	590	FEMALE	EOE	198.5	1.14	16.06	80.87

APPENDIX F: ATOMIC ABSORPTION ANALYSIS RESULTS FOR INDIVIDUAL ANIMALS

CONCENTRATION OF Cu-Zn	EXPT NUMBER	ANIMAL NUMBER	ANIMAL SEX	SACRIFICE CODE	LUNG WEIGHT IN GRAMS	MICROGRAMS METAL IN LUNG			MICROGRAMS METAL/G LUNG		
						Cu	Zn	Cu+Zn	Cu	Zn	Cu+Zn
0 (SHAM)	4370	005	M	EOE	1.15	2.99	26.8	29.8	2.59	23.3	26.0
0 (SHAM)	4370	007	M	EOE	1.15	2.20	21.3	23.5	1.91	18.4	20.3
0 (SHAM)	4370	010	M	EOE	1.15	1.88	27.5	29.4	1.63	23.8	25.5
0 (SHAM)	4370	016	M	EOE	1.15	2.57	21.9	24.4	2.23	19.0	21.2
0 (SHAM)	4370	025	M	EOE	1.15	2.08	26.0	28.1	1.80	22.6	24.4
0 (SHAM)	4370	029	M	EOE	1.15	1.97	28.3	30.2	1.71	24.5	26.2
0 (SHAM)	4370	504	F	EOE	0.89	2.73	24.7	27.4	3.07	27.8	30.8
0 (SHAM)	4370	509	F	EOE	0.89	1.67	21.9	23.5	1.88	24.6	26.5
0 (SHAM)	4370	515	F	EOE	0.89	2.75	21.7	24.5	3.09	24.4	27.5
0 (SHAM)	4370	525	F	EOE	0.89	1.14	19.8	21.0	1.28	22.3	23.6
0 (SHAM)	4370	532	F	EOE	0.89	1.90	21.1	23.0	2.14	23.7	25.8
0 (SHAM)	4370	534	F	EOE	0.89	1.53	25.3	26.8	1.72	28.4	30.2
1.0 mg/m3	4371	045	M	EOE	0.99	2.04	26.6	28.7	2.06	26.9	28.9
1.0 mg/m3	4371	053	M	EOE	1.14	2.33	21.7	24.1	2.04	19.1	21.1
1.0 mg/m3	4371	054	M	EOE	1.05	1.33	25.5	26.9	1.27	24.3	25.6
1.0 mg/m3	4371	058	M	EOE	0.99	2.52	25.5	28.0	2.55	25.7	28.3
1.0 mg/m3	4371	042	M	REC	1.12	1.13	19.2	20.3	1.01	17.1	18.1
1.0 mg/m3	4371	065	M	REC	1.16	1.10	20.8	21.9	0.95	17.9	18.9
1.0 mg/m3	4371	073	M	REC	1.14	0.69	18.7	19.4	0.61	16.4	17.0
1.0 mg/m3	4371	539	F	EOE	0.98	1.77	13.5	15.2	1.81	13.7	15.5
1.0 mg/m3	4371	561	F	EOE	0.76	1.05	12.8	13.8	1.38	16.8	18.2
1.0 mg/m3	4371	574	F	EOE	0.76	1.12	20.3	21.4	1.47	26.7	28.2
1.0 mg/m3	4371	545	F	REC	0.78	0.62	16.6	17.3	0.79	21.3	22.1
1.0 mg/m3	4371	546	F	REC	0.85	1.33	18.5	19.9	1.56	21.8	23.4
1.0 mg/m3	4371	568	F	REC	0.79	1.04	18.6	19.7	1.32	23.6	24.9

CONCENTRATION OF Cu-Zn	EXPT NUMBER	ANIMAL NUMBER	ANIMAL SEX	SACRIFICE CODE	LUNG WEIGHT IN GRAMS	MICROGRAMS METAL IN LUNG			MICROGRAMS METAL/G LUNG		
						Cu	Zn	Cu+Zn	Cu	Zn	Cu+Zn
3.2 mg/m3	4372	077	M	EOE	1.12	3.35	22.2	25.5	2.99	19.8	22.8
3.2 mg/m3	4372	091	M	EOE	1.09	4.05	18.8	22.9	3.72	17.3	21.0
3.2 mg/m3	4372	094	M	EOE	1.12	2.08	23.7	25.8	1.86	21.2	23.0
3.2 mg/m3	4372	097	M	EOE	1.09	1.97	22.5	24.4	1.81	20.6	22.4
3.2 mg/m3	4372	078	M	REC	1.17	2.43	20.4	22.9	2.08	17.5	19.5
3.2 mg/m3	4372	088	M	REC	1.12	1.22	19.0	20.2	1.09	16.9	18.0
3.2 mg/m3	4372	106	M	REC	1.11	1.06	17.4	18.4	0.95	15.7	16.6
3.2 mg/m3	4372	107	M	REC	1.06	1.38	19.6	20.9	1.30	18.5	19.8
3.2 mg/m3	4372	595	F	EOE	0.86	1.71	24.2	25.9	1.99	28.1	30.1
3.2 mg/m3	4372	596	F	EOE	0.87	1.45	17.2	18.7	1.67	19.8	21.5
3.2 mg/m3	4372	597	F	EOE	0.86	1.93	19.4	21.3	2.24	22.5	24.8
3.2 mg/m3	4372	577	F	REC	0.83	0.87	16.7	17.5	1.05	20.1	21.1
3.2 mg/m3	4372	583	F	REC	0.96	0.76	17.6	18.4	0.79	18.3	19.1
3.2 mg/m3	4372	589	F	REC	0.80	1.11	14.4	15.6	1.39	18.1	19.4
3.2 mg/m3	4372	610	F	REC	0.83	1.15	15.1	16.3	1.39	18.2	19.6
10 mg/m3	4373	120	M	EOE	1.33	2.59	23.0	25.6	1.95	17.3	19.2
10 mg/m3	4373	121	M	EOE	1.39	3.65	19.8	23.4	2.63	14.2	16.8
10 mg/m3	4373	123	M	EOE	1.23	1.98	20.3	22.3	1.61	16.5	18.1
10 mg/m3	4373	137	M	EOE	1.41	3.20	31.1	34.3	2.27	22.1	24.3
10 mg/m3	4373	115	M	REC	1.30	2.18	20.3	22.5	1.68	15.6	17.3
10 mg/m3	4373	129	M	REC	1.17	0.95	20.1	21.0	0.81	17.1	18.0
10 mg/m3	4373	131	M	REC	1.08	1.66	17.6	19.2	1.53	16.3	17.8
10 mg/m3	4373	138	M	REC	1.15	1.19	21.0	22.2	1.03	18.3	19.3
10 mg/m3	4373	621	F	EOE	0.95	2.00	20.1	22.1	2.11	21.1	23.2
10 mg/m3	4373	637	F	EOE	0.99	1.37	26.4	27.8	1.38	26.7	28.0
10 mg/m3	4373	641	F	EOE	1.02	1.64	17.1	18.7	1.61	16.8	18.4
10 mg/m3	4373	649	F	EOE	1.01	2.04	17.3	19.3	2.02	17.1	19.1
10 mg/m3	4373	619	F	REC	0.92	1.31	17.8	19.1	1.42	19.3	20.8
10 mg/m3	4373	622	F	REC	0.85	0.64	16.5	17.1	0.75	19.4	20.1
10 mg/m3	4373	645	F	REC	1.16	0.73	15.7	16.5	0.63	13.6	14.2
10 mg/m3	4373	646	F	REC	0.84	1.21	15.7	17.0	1.44	18.7	20.2

Note: For the sham-exposed rats which died prior to the last exposure lung weights used for calculation purposes were the means of the exposed rats for males and females, respectively.

APPENDIX G: RESULTS FOR INDIVIDUAL ANIMAL PULMONARY FUNCTION EVALUATIONS

TIME	EXPT	ANIMAL	GRAMS	MV	CDYN	RL	CCORD	TLC	VC	FRC	RV	DLCO	FVC	FEV1	PEFR	MMEF	EF10	SIII
BASE-1	4370	003	273	87.9	0.54	0.12	0.73	12.6	11.5	2.6	1.1	0.21	11.5	70	104.0	80.3	4.4	0.75
BASE-1	4370	007	284	84.3	0.35	0.22	0.71	12.7	11.1	2.8	1.6	0.23	11.5	70	119.8	74.2	4.2	0.84
BASE-1	4370	010	286	74.9	0.49	0.16	0.73	12.7	10.6	2.4	2.2	0.18	10.3	76	121.3	78.4	4.6	1.25
BASE-1	4370	017	266	80.9	0.38	0.17	0.64	12.1	10.5	2.5	1.6	0.20	10.4	71	101.4	70.5	3.4	1.10
BASE-1	4370	023	292	88.9	0.63	0.14	0.74	12.5	11.0	2.6	1.5	0.25	11.6	71	116.6	80.6	4.2	0.96
BASE-1	4370	025	272	83.1	0.63	0.14	0.75	12.8	10.9	2.9	2.0	0.18	11.3	67	109.4	69.3	3.9	0.58
BASE-1	4370	027	270	81.2	0.45	0.14	0.77	12.9	11.3	2.7	1.6	0.23	10.2	77	96.8	64.8	4.9	0.90
BASE-1	4370	034	277	89.4	0.41	0.29	0.72	13.0	10.5	3.3	2.5	0.20	10.6	71	108.0	73.6	3.9	0.74
BASE-1	4371	039	281	69.8	0.55	0.14	0.71	12.5	11.1	2.7	1.4	0.23	11.6	69	109.5	78.7	4.0	1.11
BASE-1	4371	041	272	94.5	0.47	0.14	0.71	12.6	11.2	2.6	1.4	0.24	11.5	70	100.0	82.6	4.5	1.02
BASE-1	4371	047	274	96.6	0.48	0.26	0.72	11.6	10.4	2.0	1.2	0.21	11.0	63	104.2	59.8	3.6	0.66
BASE-1	4371	057	266	83.8	0.33	0.22	0.69	11.8	10.5	2.0	1.2	0.22	10.7	74	109.5	82.0	4.6	1.01
BASE-1	4371	068	278	80.0	0.60	0.14	0.73	12.5	10.8	2.9	1.8	0.18	11.1	71	116.0	73.2	3.9	0.59
BASE-1	4371	069	278	72.9	0.44	0.16	0.74	12.7	10.8	2.5	2.0	0.24	11.5	71	124.0	77.9	4.3	0.94
BASE-1	4371	071	274	83.5	0.46	0.17	0.67	12.5	10.2	3.1	2.2	0.21	10.3	77	115.5	83.7	5.3	1.00
BASE-1	4371	074	271	85.8	0.72	0.02	0.70	11.9	10.9	2.2	1.0	0.24	11.2	72	106.9	80.5	4.3	1.24
BASE-1	4372	082	266	74.7	0.47	0.17	0.77	12.2	10.9	2.7	1.3	0.24	11.6	74	112.8	87.8	5.0	1.03
BASE-1	4372	083	274	71.7	0.89	0.08	0.77	13.9	10.8	3.9	3.1	0.21	11.7	64	116.9	64.9	3.7	0.55
BASE-1	4372	084	287	92.1	0.53	0.13	0.76	13.5	11.2	3.3	2.3	0.23	11.6	72	113.4	85.5	4.2	0.49
BASE-1	4372	098	295	64.7	0.63	0.14	0.74	13.1	11.3	2.7	1.7	0.23	11.6	73	117.8	86.2	4.7	0.92
BASE-1	4372	099	285	85.8	0.45	0.61	0.78	13.2	11.2	2.9	2.1	0.21	11.4	67	102.1	61.9	1.9	0.81
BASE-1	4372	105	276	77.0	0.41	0.18	0.74	12.3	11.1	2.2	1.1	0.19	11.4	74	122.5	84.3	4.4	0.80
BASE-1	4372	108	275	81.1	0.38	0.16	0.72	12.3	10.5	2.7	1.8	0.23	10.9	74	110.6	83.4	4.9	0.96
BASE-1	4372	110	283	88.1	0.43	0.15	0.73	12.5	10.9	2.7	1.5	0.22	11.3	70	111.2	74.8	4.4	1.06
BASE-1	4373	113	290	88.7	0.51	0.12	0.72	12.9	11.3	2.7	1.6	0.23	11.6	66	108.0	69.2	3.7	0.80
BASE-1	4373	118	284	78.2	0.43	0.24	0.69	12.4	10.4	2.8	2.0	0.24	10.6	69	101.6	67.9	4.3	1.24
BASE-1	4373	124	271	84.1	0.50	0.14	0.74	12.6	11.2	2.7	1.4	0.22	11.6	73	124.6	83.3	4.4	0.68
BASE-1	4373	139	276	90.8	0.38	0.15	0.75	13.0	11.1	2.9	1.9	0.24	11.6	73	111.0	85.9	4.2	1.04
BASE-1	4373	143	280	91.7	0.51	0.14	0.71	11.5	10.2	2.1	1.2	0.22	10.8	74	108.9	82.5	4.4	0.92
BASE-1	4373	145	270	83.4	0.75	0.09	0.68	11.1	10.1	2.0	1.0	0.21	10.5	64	100.0	54.7	2.8	0.94
BASE-1	4373	146	271	75.9	0.32	0.21	0.70	12.6	10.8	2.9	1.7	0.21	10.9	76	110.8	88.7	4.8	0.85
BASE-1	4373	150	271	95.6	0.27	0.19	0.69	12.0	10.8	2.4	1.1	0.21	11.1	71	110.3	77.4	4.0	0.63
BASE-1	4370	503	181	52.7	0.28	0.57	0.60	9.9	8.9	2.2	1.0	0.17	9.3	73	102.6	62.9	3.2	0.94
BASE-1	4370	508	177	67.2	0.42	0.14	0.69	11.0	9.7	2.3	1.3	0.17	10.2	75	115.2	75.7	4.5	0.85
BASE-1	4370	521	187	73.0	0.54	0.28	0.66	10.8	9.2	2.3	1.5	0.17	9.8	74	103.8	72.4	5.2	0.78
BASE-1	4370	522	177	70.2	0.34	0.15	0.54	10.0	8.8	2.1	1.2	0.18	9.2	73	98.9	66.2	4.2	1.02
BASE-1	4370	526	168	65.8	0.41	0.14	0.50	9.4	7.1	2.7	2.3	0.10	6.6	54	51.2	23.5	2.2	3.32
BASE-1	4370	529	176	65.6	0.46	0.14	0.57	9.4	8.1	1.8	1.3	0.14	8.5	77	96.8	64.8	4.9	0.96

TIME	EXPT	ANIMAL	GRAMS	MV	CDYN	RL	CCORD	TLC	VC	FRC	RV	DLCO	FVC	FEV1	PEFR	MMEF	EF10	SIII
BASE-1	4370	532	185	66.2	0.27	0.25	0.56	9.9	8.9	2.2	1.0	0.18	9.2	71	95.1	60.9	4.0	0.82
BASE-1	4370	536	179	60.6	0.30	0.16	0.56	10.0	8.8	2.2	1.3	0.13	9.2	79	106.3	77.2	6.3	0.61
BASE-1	4371	542	170	65.2	0.24	0.42	0.49	10.1	8.6	2.4	1.5	0.14	9.1	75	92.4	69.8	6.0	0.68
BASE-1	4371	551	173	80.4	0.28	0.28	0.59	10.4	9.2	2.2	1.2	0.17	8.3	50	74.6	18.5	2.6	1.14
BASE-1	4371	553	178	68.4	0.42	0.53	0.57	9.6	8.7	1.7	0.9	0.15	8.8	74	88.9	65.4	4.8	0.73
BASE-1	4371	557	171	69.5	0.40	0.08	0.60	9.3	8.7	1.6	0.6	0.15	9.1	79	105.7	76.4	5.1	1.04
BASE-1	4371	559	177	76.3	0.26	0.20	0.56	9.8	8.6	2.0	1.2	0.18	8.8	83	111.4	83.0	5.9	1.10
BASE-1	4371	565	181	76.2	0.38	0.12	0.60	11.1	9.1	2.8	2.0	0.16	9.6	82	108.1	90.7	6.1	1.32
BASE-1	4371	572	169	76.9	0.27	0.51	0.57	9.8	8.3	2.3	1.5	0.16	8.7	77	95.9	68.3	4.6	1.18
BASE-1	4371	573	176	58.4	0.38	0.17	0.55	9.4	8.4	2.0	1.0	0.12	8.7	78	94.4	71.1	4.7	0.80
BASE-1	4372	581	190	55.6	0.60	0.04	0.63	10.5	9.4	2.1	1.1	0.15	10.1	75	111.4	74.5	5.0	0.50
BASE-1	4372	582	182	73.3	0.29	0.35	0.53	10.0	8.2	2.5	1.7	0.14	8.5	37	47.7	19.1	1.9	0.93
BASE-1	4372	586	170	65.8	0.35	0.23	0.62	10.6	9.0	2.5	1.7	0.15	9.2	47	79.4	15.5	0.8	1.02
BASE-1	4372	587	180	96.5	0.32	0.20	0.57	9.5	8.3	2.0	1.2	0.16	8.6	84	104.8	83.5	6.1	1.38
BASE-1	4372	594	177	50.0	0.31	0.15	0.54	9.3	8.2	2.3	1.1	0.15	8.5	79	100.1	69.6	5.2	1.42
BASE-1	4372	601	180	56.6	0.37	0.10	0.62	10.3	9.1	2.4	1.3	0.15	9.4	80	102.8	82.2	5.4	0.79
BASE-1	4372	607	176	58.0	0.48	0.16	0.55	9.1	8.1	2.0	1.0	0.13	8.3	78	95.4	65.6	5.1	1.44
BASE-1	4372	611	173	76.0	0.32	0.18	0.54	9.4	8.3	1.9	1.2	0.16	8.4	80	92.2	73.3	5.2	1.16
BASE-1	4373	613	184	72.5	0.31	0.20	0.61	9.9	8.4	2.2	1.5	0.17	8.7	64	88.8	35.9	1.5	1.27
BASE-1	4373	614	178	71.0	0.26	0.28	0.48	9.6	8.6	2.1	1.0	0.18	8.6	38	58.2	10.1	1.5	1.49
BASE-1	4373	623	189	75.4	0.44	0.12	0.61	10.7	9.7	2.0	1.0	0.17	10.0	74	105.6	71.7	4.5	1.15
BASE-1	4373	629	176	49.9	0.23	0.25	0.51	9.5	8.4	2.4	1.0	0.12	8.9	86	107.6	90.2	6.6	0.78
BASE-1	4373	635	172	51.1	0.39	0.22	0.60	10.4	8.9	2.4	1.5	0.13	9.1	76	91.8	71.3	4.5	0.70
BASE-1	4373	640	175	82.0	0.40	0.11	0.49	9.7	8.4	2.3	1.4	0.16	8.8	83	109.2	82.4	5.9	1.12
BASE-1	4373	644	183	67.3	0.38	0.08	0.60	11.0	9.0	3.0	2.0	0.15	9.3	78	89.8	78.6	5.7	1.03
BASE-1	4373	647	181	64.5	0.41	0.11	0.53	9.1	8.2	1.8	0.9	0.16	8.6	85	110.6	83.8	6.0	1.16
MID-1	4370	003	286	92.0	0.30	0.18	0.80	13.1	12.4	2.2	0.7	0.23	12.7	69	118.5	84.1	18.0	0.48
MID-1	4370	007	286	82.0	0.38	0.17	0.82	12.8	12.3	2.3	0.6	0.26	13.0	68	126.4	85.8	23.0	0.51
MID-1	4370	010	294	100.3	0.60	0.10	0.78	12.7	11.9	2.3	0.8	0.24	12.5	68	126.4	78.1	27.0	0.72
MID-1	4370	017	276	94.9	0.74	0.12	0.73	12.9	12.1	2.4	0.7	0.25	12.1	70	101.9	89.8	25.0	0.52
MID-1	4370	023	302	81.9	0.54	0.13	0.84	13.6	12.7	2.7	1.0	0.27	13.5	69	135.7	91.6	19.0	0.57
MID-1	4370	025	281	83.6	0.56	0.09	0.73	12.3	11.3	2.4	1.1	0.22	11.8	71	116.9	82.6	20.0	0.72
MID-1	4370	027	287	64.8	0.64	0.06	0.85	13.3	12.9	2.3	0.4	0.21	13.7	67	128.6	83.7	14.0	0.55
MID-1	4370	034	296	89.5	0.73	0.08	0.72	12.8	11.5	2.5	1.3	0.23	12.9	62	110.4	74.9	5.0	0.53
MID-1	4371	039	290	78.6	0.74	0.09	0.75	12.9	11.6	2.3	1.3	0.24	12.3	66	109.3	77.1	16.0	0.84
MID-1	4371	041	292	77.0	0.40	0.16	0.79	13.2	12.6	2.6	0.6	0.26	13.9	63	110.5	85.0	14.0	0.60
MID-1	4371	047	279	75.9	0.38	0.15	0.73	13.0	11.7	2.9	1.3	0.23	12.8	63	111.7	72.7	14.0	0.52
MID-1	4371	057	270	67.5	0.34	0.18	0.75	11.6	11.1	2.0	0.5	0.25	12.3	70	114.0	85.7	10.0	0.53
MID-1	4371	068	280	58.1	0.35	0.20	0.76	12.8	11.8	2.2	1.0	0.25	12.8	67	109.0	89.1	18.0	0.50
MID-1	4371	069	289	79.1	0.38	0.15	0.84	13.6	12.6	2.4	1.0	0.27	13.4	68	118.1	88.6	11.0	0.48
MID-1	4371	071	274	97.8	0.60	0.07	0.73	12.4	10.9	2.4	1.5	0.25	11.6	70	119.4	76.9	16.0	1.05

TIME	EXPT	ANIMAL	GRAMS	MV	CDYN	RL	CCORD	TLC	VC	FRC	RV	DLCO	FVC	FEV1	PEFR	MMEF	E 10	SIII
MID-1	4371	074	279	78.2	0.44	0.17	0.79	13.3	12.0	2.5	1.3	0.25	12.3	69	106.9	88.3	22.0	0.79
MID-1	4372	082	267	93.3	0.52	0.14	0.82	13.5	12.4	2.6	1.1	0.28	11.8	47	73.8	36.4	10.0	0.91
MID-1	4372	083	281	78.6	0.56	0.17	0.85	13.5	13.0	2.4	0.5	0.29	13.4	59	107.4	76.5	26.0	0.55
MID-1	4372	084	301	99.0	0.62	0.06	0.68	12.4	11.8	1.8	0.6	0.22	12.5	62	119.4	64.9	25.0	0.56
MID-1	4372	098	309	84.6	0.43	0.15	0.84	13.8	12.8	2.6	1.0	0.24	13.5	72	133.4	97.0	17.0	0.54
MID-1	4372	099	290	101.1	0.68	0.08	0.78	13.8	12.5	2.8	1.3	0.29	13.2	67	111.0	89.6	17.0	0.87
MID-1	4372	105	282	85.9	0.55	0.10	0.78	12.9	12.1	2.3	0.8	0.20	12.9	71	127.2	90.3	18.0	0.59
MID-1	4372	108	286	80.0	0.63	0.23	0.78	13.4	12.6	2.4	0.9	0.24	12.7	67	112.7	86.4	24.0	0.72
MID-1	4372	110	304	86.0	0.35	0.21	0.75	13.2	12.3	2.5	0.9	0.26	13.7	63	117.6	82.0	12.0	0.96
MID-1	4373	113	294	88.8	0.39	0.17	0.68	12.3	11.0	2.5	1.2	0.22	11.5	64	110.4	58.6	15.0	1.02
MID-1	4373	118	305	92.3	0.54	0.09	0.76	12.4	11.5	2.3	0.9	0.23	12.0	64	111.2	70.0	22.0	0.77
MID-1	4373	124	286	75.5	0.48	0.12	0.75	12.4	11.2	2.1	1.2	0.18	12.1	75	124.4	95.1	16.0	0.51
MID-1	4373	139	283	78.3	0.45	0.13	0.67	12.3	10.9	3.0	1.3	0.22	11.7	70	107.3	83.9	20.0	0.95
MID-1	4373	143	286	79.0	0.52	0.09	0.74	11.7	11.3	2.1	0.4	0.21	11.7	67	115.8	71.5	23.0	0.92
MID-1	4373	145	285	84.4	0.40	0.14	0.73	11.8	11.1	2.0	0.6	0.24	12.1	69	113.4	79.9	15.0	0.76
MID-1	4373	146	271	70.6	0.32	0.23	0.57	11.6	10.2	3.2	1.4	0.24	11.8	71	112.5	84.5	7.0	1.15
MID-1	4373	150	284	87.0	0.55	0.12	0.72	12.7	11.4	2.8	1.3	0.22	12.5	63	112.3	66.2	14.0	0.52
MID-1	4370	503	184	69.0	0.26	0.26	0.62	10.0	9.3	1.8	0.8	0.17	10.4	78	115.4	87.2	10.0	0.99
MID-1	4370	508	183	66.8	0.22	0.25	0.63	10.6	9.8	1.9	0.7	0.17	10.1	71	110.4	68.8	23.0	0.82
MID-1	4370	521	190	81.4	0.34	0.21	0.63	10.7	9.8	2.2	0.9	0.23	10.3	78	115.2	86.7	18.0	0.92
MID-1	4370	522	175	75.5	0.32	0.21	0.66	11.3	10.4	2.4	1.0	0.20	11.1	72	116.2	77.2	14.0	0.69
MID-1	4370	526	166	85.5	0.41	0.14	0.54	9.3	8.9	1.7	0.5	0.16	9.3	61	87.4	37.4	4.0	0.94
MID-1	4370	529	175	79.6	0.26	0.22	0.54	9.1	8.6	1.7	0.5	0.16	8.8	80	104.5	71.4	20.0	1.17
MID-1	4370	532	186	67.6	0.53	0.11	0.65	10.8	9.7	2.1	1.1	0.21	10.1	75	105.2	79.5	20.0	0.88
MID-1	4370	536	177	74.2	0.38	0.18	0.58	9.8	9.1	1.9	0.7	0.15	9.9	74	108.3	73.2	14.0	1.11
MID-1	4371	542	173	63.9	0.24	0.23	0.54	9.5	8.8	2.0	0.7	0.15	9.3	80	104.0	78.4	23.0	0.98
MID-1	4371	551	181	87.6	0.30	0.23	0.59	10.4	9.7	1.9	0.7	0.17	10.8	75	112.0	82.2	9.0	0.84
MID-1	4371	553	180	68.3	0.34	0.21	0.50	9.2	8.0	2.0	1.2	0.17	8.7	44	54.9	20.5	6.0	1.04
MID-1	4371	557	173	72.0	0.37	0.19	0.58	9.8	9.1	1.8	0.7	0.16	9.9	63	92.2	49.1	6.0	0.89
MID-1	4371	559	177	80.2	0.27	0.21	0.51	9.3	8.8	1.8	0.5	0.19	9.4	79	110.3	78.8	14.0	1.10
MID-1	4371	565	182	57.6	0.61	0.06	0.56	10.8	9.4	2.9	1.4	0.17	10.4	80	120.1	91.0	16.0	1.15
MID-1	4371	572	165	62.4	0.30	0.25	0.52	9.2	8.6	1.6	0.6	0.16	9.4	76	97.2	76.5	14.0	1.01
MID-1	4371	573	180	70.0	0.43	0.10	0.59	10.6	9.6	2.0	1.0	0.17	10.1	77	112.3	82.1	26.0	0.90
MID-1	4372	581	194	58.5	0.45	0.11	0.65	11.7	10.5	2.6	1.2	0.21	11.0	70	111.0	76.8	24.0	0.75
MID-1	4372	582	178	67.0	0.35	0.19	0.66	10.3	10.0	1.7	0.4	0.17	10.8	70	107.8	71.5	12.0	0.71
MID-1	4372	586	175	50.8	0.37	0.22	0.65	11.1	9.6	2.6	1.6	0.17	10.3	54	83.3	29.3	7.0	0.82
MID-1	4372	587	177	85.0	0.34	0.20	0.62	10.1	9.4	1.9	0.6	0.19	9.6	79	107.2	78.6	17.0	0.74
MID-1	4372	594	174	69.3	0.26	0.25	0.60	9.3	8.6	1.9	0.7	0.16	8.4	62	67.3	44.4	18.0	1.14
MID-1	4372	601	170	66.5	0.27	0.21	0.49	9.5	8.6	2.3	0.9	0.16	8.8	85	110.5	86.2	19.0	1.03
MID-1	4372	607	178	63.5	0.31	0.23	0.54	9.5	8.6	2.0	0.9	0.18	9.2	77	101.3	75.1	14.0	0.83
MID-1	4372	611	168	66.9	0.67	0.12	0.52	9.2	8.5	1.7	0.6	0.15	9.3	74	94.6	73.3	15.0	0.98

TIME	EXPT	ANIMAL	GRAMS	MV	CDYN	RL	CCORD	TLC	VC	FRC	RV	DLCO	FVC	FEV1	PEFR	MMEF	EF10	SIII
MID-1	4373	613	185	85.5	0.33	0.16	0.56	9.5	8.6	2.0	0.8		8.9	82	105.9	84.2	11.0	0.98
MID-1	4373	614	188	80.3	0.25	0.27	0.58	9.6	8.8	2.0	0.8	0.16	9.2	79	106.6	80.7	17.0	0.70
MID-1	4373	623	190	67.9	0.30	0.19	0.60	10.6	9.6	2.2	1.0	0.17	10.0	78	112.4	84.2	2[illegible].0	1.01
MID-1	4373	629	181	68.8	0.34	0.19	0.54	9.9	8.7	2.3	1.2	0.16	9.4	81	112.4	84.7	12.0	1.00
MID-1	4373	635	176	67.5	0.30	0.17	0.61	9.7	9.3	1.8	0.4	0.14	9.5	77	97.9	79.8	21.0	0.73
MID-1	4373	640	187	74.3	0.37	0.13	0.56	9.9	9.1	2.1	0.8	0.17	9.7	77	107.2	78.8	15.0	0.59
MID-1	4373	644	180	68.9	0.28	0.22	0.61	10.6	9.4	2.3	1.2	0.18	10.3	72	99.0	78.8	12.0	0.68
MID-1	4373	647	178	69.0	0.34	0.22	0.60	10.1	8.9	2.3	1.2	0.16	9.6	74	109.7	68.7	15.0	0.74
EOE-1	4371	039	309	112.5	0.60	0.14	0.86	14.1	11.9	2.4	2.3	0.29	12.9	67	118.4	80.8	12.0	0.50
EOE-1	4371	041	313	65.9	0.42	0.18	0.84	14.2	13.2	2.9	1.0	0.23	13.9	65	118.0	89.2	23.0	0.41
EOE-1	4371	047	289	111.1	0.42	0.19	0.83	13.2	12.3	2.5	0.9	0.20	12.9	66	117.0	81.0	16.0	0.39
EOE-1	4371	057	299	142.9	0.36	0.21	0.83	13.4	13.1	2.2	0.3	0.20	13.4	68	124.8	91.3	25.0	0.42
EOE-1	4371	068	307	53.8	0.36	0.17	0.76	13.2	12.3	2.4	0.9	0.27	12.8	68	125.7	80.0	19.0	0.48
EOE-1	4371	069	311	103.2	0.38	0.25	0.88	14.0	13.2	2.4	0.8	0.20	13.8	65	121.6	82.3	22.0	0.48
EOE-1	4371	071	304	104.8	0.31	0.18	0.76	11.7	10.6	2.1	1.1	0.27	11.6	69	108.1	76.9	14.0	0.54
EOE-1	4371	074	309	99.4	0.41	0.07	0.73	11.5	11.5	1.8	0.0	0.29	11.7	75	119.8	91.9	24.0	0.61
EOE-1	4372	082	300	140.4	0.65	0.10	0.88	14.6	13.6	2.8	1.0	0.22	14.3	62	125.7	81.6	31.0	0.42
EOE-1	4372	083	310	118.7	0.67	0.13	0.99	14.3	14.1	2.7	0.3	0.33	14.1	62	121.1	80.2	18.0	0.42
EOE-1	4372	084	329	93.5	0.67	0.11	0.92	14.6	13.8	2.5	0.9	0.24	14.3	62	119.7	81.3	18.0	0.43
EOE-1	4372	098	336	111.0	0.38	0.20	0.87	13.1	12.8	2.1	0.3	0.34	13.3	66	126.8	79.3	25.0	0.56
EOE-1	4372	099	308	113.5	0.55	0.10	0.96	13.4	13.1	2.5	0.3	0.34	13.6	57	109.0	42.8	3.0	0.35
EOE-1	4372	105	328	113.0	0.49	0.09	0.80	13.3	12.5	2.2	0.8	0.32	12.9	64	124.8	73.5	24.0	0.63
EOE-1	4372	108	310	123.7	0.43	0.14	0.81	12.7	12.2	2.0	0.5	0.32	12.9	69	127.0	82.8	28.0	0.55
EOE-1	4372	110	315	125.5	0.34	0.25	0.85	14.5	13.1	2.6	1.3	0.37	13.5	63	117.6	78.4	28.0	0.38
EOE-1	4373	113	291	120.0	0.71	0.10	0.73	12.5	12.0	2.4	0.5	0.20	12.5	60	109.2	58.9	11.0	0.42
EOE-1	4373	118	329	118.8	0.45	0.13	0.78	13.0	11.7	2.4	1.2	0.32	12.0	65	111.8	70.1	20.0	0.50
EOE-1	4373	124	295	104.8	0.29	0.21	0.77	12.9	11.6	2.4	1.2	0.23	12.4	75	119.0	104.3	17.0	0.58
EOE-1	4373	139	310	88.3	0.38	0.18	0.78	12.9	12.1	2.4	0.8	0.27	12.5	69	112.3	87.3	21.0	0.45
EOE-1	4373	143	304	108.8	0.41	0.18	0.77	11.8	11.1	2.1	0.7	0.19	11.8	65	118.6	67.0	25.0	0.59
EOE-1	4373	145	295	117.6	0.41	0.22	0.75	12.7	11.5	2.7	1.2	0.18	12.2	38	83.4	16.1	4.0	0.49
EOE-1	4373	146	286	115.1	0.27	0.22	0.88	13.4	11.5	2.5	1.9	0.25	14.3	62	125.7	81.6	31.0	0.54
EOE-1	4373	150	303	117.9	0.57	0.15	0.88	13.1	12.6	2.2	0.5	0.25	12.7	58	107.0	55.5	19.0	0.48
EOE-1	4371	542	182	83.1	0.52	0.15	0.65	10.3	9.7	1.9	0.6	0.16	10.2	69	87.4	67.3	9.0	0.70
EOE-1	4371	551	181	92.6	0.48	0.14	0.65	10.9	10.0	1.9	0.9	0.20	10.7	53	86.2	39.6	5.0	1.12
EOE-1	4371	553	185	75.9	0.49	0.19	0.63	10.5	9.4	2.1	1.0	0.19	10.0	79	106.4	87.3	22.0	0.86
EOE-1	4371	557	184	76.8	0.39	0.19	0.60	9.5	8.9	1.8	0.6	0.17	9.4	57	70.0	42.4	16.0	0.96
EOE-1	4371	559	189	106.5	0.28	0.30	0.55	9.3	9.0	1.4	0.3	0.19	9.3	78	106.0	78.5	18.0	0.91
EOE-1	4371	565	190	107.5	0.26	0.23	0.60	10.7	10.0	2.1	0.7	0.22	10.5	76	111.2	82.6	22.0	0.68
EOE-1	4371	572	184	90.9	0.34	0.22	0.59	9.5	9.0	1.6	0.5	0.21	8.7	48	65.9	22.5	6.0	1.03
EOE-1	4371	573	185	67.3	0.30	0.15	0.67	10.9	9.9	2.1	1.0	0.20	10.6	77	119.3	86.5	23.0	0.69
EOE-1	4372	581	205	95.5	0.56	0.09	0.73	11.5	11.0	2.0	0.5	0.21	11.6	63	96.2	64.2	15.0	0.56

TIME	EXPT	ANIMAL	GRAMS	MV	CDYN	RL	CCORD	TLC	VC	FRC	RV	DLCO	FVC	FEV1	PEFR	MMEF	:F10	SIII
EOE-1	4372	582	190	78.1	0.33	0.24	0.74	10.6	10.2	1.9	0.4	0.21	10.4	57	79.1	43.1	7.0	0.68
EOE-1	4372	586	185	113.1	0.38	0.17	0.67	11.1	9.7	2.3	1.5	0.18						0.59
EOE-1	4372	587	184	81.0	0.59	0.16	0.68	10.1	9.5	1.5	0.6	0.15	10.0	56	85.4	40.0	15.0	1.19
EOE-1	4372	594	186	67.0	0.38	0.21	0.57	9.6	9.2	1.8	0.4	0.18	9.6	70	99.3	61.5	8.0	1.36
EOE-1	4372	601	191	67.0	0.38	0.21	0.57	9.8	9.2	1.9	0.6	0.17	9.6	70	99.3	61.6	8.0	1.35
EOE-1	4372	607	185	130.5	0.29	0.24	0.60	9.7	9.1	1.9	0.7	0.16	9.4	78	104.8	77.0	18.0	0.82
EOE-1	4372	611	181	66.3	0.43	0.10	0.63	9.6	9.1	1.6	0.5	0.19	9.3	70	104.0	68.5	18.0	0.83
EOE-1	4373	613	187	101.9	0.31	0.10	0.46	8.1	7.5	1.7	0.6	0.15	8.3	74	74.5	61.4	20.0	1.42
EOE-1	4373	614	186	99.1	0.30	0.18	0.50	9.1	8.7	2.0	0.4	0.16	9.3	72	87.1	64.5	18.0	0.72
EOE-1	4373	623	198	112.2	0.32	0.52	0.59	9.8	8.8	1.9	1.0	0.19	9.2	70	89.9	62.4	20.0	0.99
EOE-1	4373	629	182	68.9	0.26	0.27	0.62	9.4	8.7	1.8	0.6	0.14	9.2	75	102.6	70.2	16.0	0.81
EOE-1	4373	635	179	59.5	0.42	0.14	0.58	9.9	9.3	1.9	0.7	0.15	9.5	58	68.5	43.1	13.0	0.62
EOE-1	4373	640	190	120.0	0.28	0.40	0.63	10.0	9.2	1.8	0.7	0.16	9.8	74	97.2	72.6	11.0	0.70
EOE-1	4373	644	192	70.3	0.38	0.15	0.59	11.0	9.9	2.1	1.2	0.15	10.5	52	81.4	40.2	13.0	0.80
EOE-1	4373	647	188	78.4	0.23	0.27	0.59	9.7	8.8	1.8	0.9	0.15	9.2	70	89.9	62.4	20.0	0.99
REC-1	4371	039	331	71.0	0.28	0.33	0.84	12.2	11.3	2.3	0.9	0.23	12.9	65	119.8	75.2	19.0	0.55
REC-1	4371	041	329	88.8	0.49	0.16	0.88	15.4	13.6	3.7	1.8	0.19	15.6	64	140.6	84.7	24.0	0.48
REC-1	4371	047	314	90.8	0.69	0.10	0.77	13.3	11.6	2.6	1.7	0.22	12.8	56	108.5	56.6	23.0	0.68
REC-1	4371	057	332	80.9	0.50	0.13	0.95	14.8	13.9	2.7	0.9	0.22	14.8	62	135.4	80.5	32.0	0.38
REC-1	4371	068	327	71.1	0.78	0.06	0.86	16.2	12.8	3.6	2.4	0.32	14.4	66	127.5	90.1	18.0	0.41
REC-1	4371	069	359	91.1	0.40	0.12	0.88	15.0	13.1	3.2	1.8	0.37	14.5	60	124.9	73.7	13.0	0.42
REC-1	4371	071	336	94.8	0.56	0.05	0.78	13.3	11.5	2.7	1.8	0.32	13.1	66	126.8	78.0	23.0	0.50
REC-1	4371	074	331	86.2	0.33	0.26	0.80	12.0	11.1	2.0	0.9	0.20	12.8	58	106.7	62.5	21.0	0.35
REC-1	4372	082	329	53.6	0.50	0.13	0.79	16.3	15.2	3.4	1.2	0.19	16.2	61	132.3	92.2	27.0	0.53
REC-1	4372	083	334	92.6	0.66	0.08	0.98	16.5	14.7	3.1	1.9	0.24	15.8	63	133.3	96.6	25.0	0.27
REC-1	4372	084	351	83.4	0.59	0.12	0.93	16.4	14.0	3.2	2.4	0.21	15.7	59	133.4	79.8	29.0	0.42
REC-1	4372	098	350	74.3	0.50	0.14	1.00	15.5	14.1	2.8	1.4	0.22	15.0	66	145.5	91.5	26.0	0.49
REC-1	4372	099	335	103.0	0.71	0.15	0.87	14.5	13.4	3.0	1.1	0.16	14.7	67	122.4	102.6	32.0	0.56
REC-1	4372	105	345	78.5	0.75	0.07	0.91	15.3	13.6	3.2	1.7	0.20	14.8	59	129.2	73.9	26.0	0.98
REC-1	4372	108	325	66.7	0.45	0.11	0.97	15.2	13.7	3.1	1.4	0.20	15.2	63	140.1	82.6	28.0	0.39
REC-1	4372	110	345	89.8	0.62	0.05	0.60	14.9	13.3	3.2	1.6	0.11	14.8	64	138.6	86.2	13.0	0.60
REC-1	4373	113	332	79.0	0.63	0.05	0.82	14.3	12.4	3.2	2.0	0.31	14.1	57	116.2	65.0	16.0	0.45
REC-1	4373	118	370	120.1	0.34	0.19	0.95	14.6	13.3	3.0	1.3	0.23	14.2	59	111.1	73.8	13.0	0.40
REC-1	4373	124	333	108.5	0.67	0.13	1.06	16.0	15.1	2.8	1.0	0.20	16.5	66	159.2	101.1	33.0	0.32
REC-1	4373	139	343	85.0	0.54	0.11	0.80	13.5	11.7	3.4	1.8	0.33	12.8	69	125.8	84.5	25.0	0.70
REC-1	4373	143	347	96.7	0.31	0.18	0.85	13.9	12.4	2.5	1.4	0.21	13.9	66	136.8	82.9	25.0	0.42
REC-1	4373	145	321	89.4	0.34	0.19	0.90	12.9	11.4	2.8	1.5	0.20	12.5	70	123.5	85.1	17.0	0.73
REC-1	4373	146	309	73.9	0.46	0.12	0.80	13.9	12.3	3.0	1.6	0.25	13.3	72	126.4	98.4	27.0	0.51
REC-1	4373	150	335	96.7	0.71	0.09	0.90	15.3	13.8	3.2	1.5	0.21	15.1	61	132.4	79.9	11.0	0.31
REC-1	4371	542	194	85.3	0.43	0.07	0.64	10.4	10.0	2.1	0.4	0.24	10.8	78	116.9	91.2	25.0	0.57
REC-1	4371	551	205	71.8	0.29	0.20	0.73	12.3	10.5	2.4	1.7	0.16	11.6	71	122.0	78.7	17.0	0.64

TIME	EXPT	ANIMAL	GRAMS	MV	CDYN	RL	CCORD	TLC	VC	FRC	RV	DLCO	FVC	FEV1	PEFR	MMEF	EF10	SIII
REC-1	4371	553	198	86.2	0.47	0.15	0.67	11.4	10.4	2.8	1.0	0.19	11.2	73	108.0	82.9	24.0	1.13
REC-1	4371	557	197	53.6	0.51	0.09	0.69	11.2	9.6	2.5	1.6	0.21	10.9	73	115.5	78.4	21.0	0.70
REC-1	4371	559	197	77.0	0.34	0.15	0.64	10.3	9.2	2.4	1.1	0.22	10.0	77	115.6	81.7	25.0	0.81
REC-1	4371	565	204	79.4	0.32	0.19	0.67	12.9	11.0	2.9	1.9	0.21	11.9	73	130.6	85.6	23.0	0.84
REC-1	4371	572	192	64.5	0.19	0.32	0.51	9.5	8.3	2.3	1.1	0.20	9.1	68	96.0	55.4	7.0	0.85
REC-1	4371	573	192	48.5	0.30	0.21	0.74	11.3	9.8	2.6	1.5	0.10	10.7	76	109.4	87.3	23.0	0.80
REC-1	4371	581	220	74.0	0.31	0.19	0.81	11.9	11.2	2.4	0.7	0.19	12.0	73	124.2	88.9	22.0	0.74
REC-1	4372	582	203	72.9	0.21	0.39	0.57	9.5	8.6	1.7	0.9	0.19	9.6	53	84.2	24.5	8.0	0.86
REC-1	4372	586	190	53.6	0.61	0.09	0.63	10.2	9.1	2.2	1.1	0.18	9.9	75	110.2	75.4	26.0	0.00
REC-1	4372	587	196	92.6	0.23	0.26	0.69	11.2	9.5	2.2	1.7	0.17	10.8	78	115.1	91.0	[illegible]	0.83
REC-1	4372	594	195	74.1	0.26	0.25	0.65	10.5	9.5	2.0	1.0	0.14	10.4	81	121.3	93.9	[illegible]	0.97
REC-1	4372	601	196	96.3	0.27	0.22	0.72	11.6	9.3	2.9	2.3	0.19	9.5	55	77.7	35.8	10.0	0.94
REC-1	4372	607	198	74.4	0.27	0.25	0.60	9.9	8.8	2.2	1.1	0 24	9.5	79	103 5	79.7	18.0	0.47
REC-1	4372	611	186	52.3	0.31	0.10	0.65	10.5	9.0	2.4	1.5	0.16	10.3	50	65.6	40.4	19.0	0.65
REC-1	4373	613	199	79.6	0.36	0.21	0.65	10.2	9.4	2.2	0.8	0.18	10.1	76	111.2	77.2	23.0	0.40
REC-1	4373	614	197	76.8	0.28	0.14	0.68	11.0	9.5	2.7	1.5	0.17	10.3	77	103.1	83.7	23.0	0.62
REC-1	4373	623	214	105.7	0.32	0.15	0.80	12.3	11.1	2.5	1.2	0.18	11.8	72	123.4	84.7	25.0	0.72
REC-1	4373	629	199	74.1	0.22	0.26	0.62	10.7	9.0	2.6	1.7	0.23	10.2	79	109.6	92.4	21.0	0.94
REC-1	4373	635	193	54.9	0.35	0.14	0.65	11.5	9.9	2.4	1.6	0.14	10.9	77	122.0	85.8	20.0	0.63
REC-1	4373	640	202	69.7	0.29	0.18	0.62	10.5	9.2	2.3	1.3	0.22	10.3	81	123.7	93.1	22.0	0.70
REC-1	4373	644	202	66.7	0.32	0.19	0.76	11.8	10.3	2.5	1.5	0.17	11.4	78	122.2	95.7	28.0	0.68
REC-1	4373	647	197	75.1	0.28	0.19	0.65	10.7	9.5	2.5	1.2	0.23	10.3	72	115.7	72.1	22.0	0.62
BASE-2	4442	101	288	85.6	0.65	0.03	0.58	11.2	10.0	2.3	1.1	0.24	10.7	70	101.7	72.7	20.0	0.65
BASE-2	4442	102	300	79.3	0.64	0.07	0.53	11.5	9.6	2.6	1.9	0.19	9.9	70	99.2	65.6	26.0	0.70
BASE-2	4442	103	296	90.9	0.61	0.06	0.57	10.4	9.7	1.9	0.6	0.22	9.1	75	95.9	71.4	22.0	0.89
BASE-2	4442	104	287	96.3	0.29	0.19	0.66	10.4	10.6	2.1	0.6	0.26	10.2	74	111.6	75.4	24.0	0.51
BASE-2	4442	105	282	69.6	0.48	0.09	0.46	9.9	9.0	2.0	0.8	0.24	8.9	76	89.9	72.6	15.0	0.63
BASE-2	4442	106	302	87.2	0.69	0.04	0.65	11.6	10.5	2.2	1.0	0.21	9.9	72	98.9	70.9	26.0	0.72
BASE-2	4442	107	292	72.1	0.35	0.20	0.60	10.0	10.4	1.5	0.2	0.23	10.3	70	102.7	71.8	18.0	0.59
BASE-2	4442	108	295	67.1	0.64	0.13	0.58	10.2	8.9	1.8	1.4	0.14	9.0	67	97.8	51.1	20.0	0.56
BASE-2	4444	161	299	83.1	0.58	0.05	0.65	11.6	10.7	1.9	0.9	0.19	10.4	66	105.9	58.9	22.0	0.65
BASE-2	4444	162	288	71.1	0.51	0.10	0.59	9.8	9.0	1.5	0.8	0.19	9.5	72	99.5	66.2	18.0	0.72
BASE-2	4444	163	291	82.6	0.41	0.08	0.67	10.8	10.2	1.9	0.6	0.21	9.9	77	105.1	83.3	21.0	0.71
BASE-2	4444	164	303	80.8	0.61	0.07	0.54	10.6	9.4	2.2	1.3	0.23	10.3	73	97.7	78.7	25.0	0.54
BASE-2	4444	165	305	86.1	1.19	0.01	0.60	11.0	10.1	1.9	1.0	0.22	9.8	69	98.4	63.2	19.0	0.91
BASE-2	4444	166	290	78.8	0.47	0.14	0.61	11.2	10.5	2.3	0.8	0.25	10.3	71	96.8	74.0	19.0	0.97
BASE-2	4444	167	302	89.3	0.60	0.11	0.74	12.9	11.6	2.4	1.2	0.25	11.4	67	99.6	71.3	19 0	0.54
BASE-2	4444	168	309	88.3	0.52	0.12	0.73	12.5	11.5	2.4	1.0	0.22	10.9	72	95.4	85.7	26.0	0.49
BASE-2	4442	501	175	52.2	0.20	0.28	0.50	8.1	7.6	1.7	0.4	0.14	7.4	84	93.8	72.6	16.0	0.90
BASE-2	4442	502	181	66.8	0.31	0.19	0.41	7.0	6.2	1.6	0.8	0.14	6.7	84	82.1	63.0	17.0	0.81
BASE-2	4442	503	191	64.3	0.52	0.09	0.53	8.9	8.1	2.0	0.8	0.16	[illegible]	79	96.8	66.0	22.0	0.76

TIME	EXPT	ANIMAL	GRAMS	MV	CDYN	RL	CCORD	TLC	VC	FRC	RV	DLCO	FVC	FEV1	PEFR	MMEF	FF10	SIII
BASE-2	4442	504	171	67.1	0.28	0.21	0.53	9.3	8.3	1.9	1.0	0.11	7.8	81	95.3	67.9	18.0	0.73
BASE-2	4442	505	193	61.7	0.48	0.11	0.57	9.5	8.7	2.1	0.8	0.19	8.2	74	83.6	58.9	18.0	0.47
BASE-2	4442	506	181	63.7	0.25	0.26	0.36	7.4	6.3	1.6	1.1	0.16	4.6	71	49.8	30.8	13.0	0.70
BASE-2	4442	507	178	81.4	0.25	0.27	0.54	9.1	8.1	2.0	0.9	0.18	8.1	79	90.0	70.3	20.0	0.69
BASE-2	4442	508	173	68.5	0.25	0.22	0.41	7.5	6.6	1.6	0.9	0.15	7.0	86	94.2	74.1	16.0	0.72
BASE-2	4444	561	177	58.5	0.26	0.26	0.50	9.3	8.1	1.9	1.2	0.16	8.2	80	94.2	71.7	17.0	0.76
BASE-2	4444	562	173	58.6	0.34	0.14	0.55	9.5	8.7	2.2	0.8	0.15	8.3	79	97.0	67.3	19.0	0.65
BASE-2	4444	563	175	45.1	0.14	0.13	0.48	9.1	7.4	2.5	1.6	0.13	7.6	75	80.6	58.0	14.0	0.73
BASE-2	4444	564	179	58.2	0.70	0.14	0.58	9.7	8.7	2.1	1.0	0.23	8.9	72	76.9	67.6	22.0	0.60
BASE-2	4444	565	186	96.3	0.29	0.19	0.44	9.0	8.1	2.0	0.9	0.16	8.3	81	90.9	77.8	22.0	0.64
BASE-2	4444	566	182	45.8	0.34	0.18	0.46	8.4	7.3	1.9	1.1	0.13	7.6	82	94.8	68.8	19.0	0.36
BASE-2	4444	567	181	98.6	0.21	0.36	0.32	10.1	5.9	4.5	4.2	0.11	6.1	43	32.3	13.0	3.0	0.64
BASE-2	4444	568	183	41.8	0.28	0.17	0.53	9.2	7.6	2.3	1.6	0.12	7.1	62	56.2	39.1	16.0	0.65
MID-2	4442	101	294	74.2	0.49	0.09	0.65	12.2	11.1	2.9	1.1	0.24	11.6	70	112.0	80.7	21.0	0.58
MID-2	4442	102	310	109.7	0.71	0.04	0.96	19.1	18.5	3.7	0.5	0.26	17.7	70	177.7	123.5	41.0	0.48
MID-2	4442	103	303	90.8	0.48	0.11	0.82	13.4	12.5	2.6	0.9	0.25	12.4	68	115.5	57.5	24.0	0.64
MID-2	4442	104	303	105.2	0.53	0.09	0.75	13.2	12.0	2.8	1.2	0.28	11.9	67	118.2	72.6	27.0	0.83
MID-2	4442	105	297	101.1	0.52	0.27	1.11	18.5	17.2	4.0	1.3	0.23	16.9	67	137.1	112.1	32.0	0.63
MID-2	4442	106	322	161.7	0.80	0.05	1.13	18.2	17.3	3.1	0.9	0.23	16.1	65	148.1	91.8	29.0	0.44
MID-2	4442	107	309	55.9	0.50	0.12	0.79	12.4	11.3	2.4	1.1	0.23	12.2	67	111.0	76.5	19.0	0.68
MID-2	4442	108	329	87.4	0.61	0.08	0.74	12.2	11.3	2.3	0.9	0.23	11.9	61	111.7	63.4	24.0	0.50
MID-2	4444	161	290	81.6	0.59	0.10	0.77	13.4	12.1	2.6	1.3	0.23	11.8	69	117.7	77.8	24.0	0.38
MID-2	4444	162	294	118.0	0.75	0.09	1.14	18.3	16.9	3.2	1.4	0.24	16.4	73	168.4	121.5	33.0	0.60
MID-2	4444	163	298	89.7	0.39	0.12	0.92	15.3	13.3	3.2	2.0	0.28	13.2	64	123.9	78.6	26.0	0.58
MID-2	4444	164	310	89.0	0.39	0.21	0.48	13.8	12.5	2.7	1.3	0.29	12.3	66	110.3	77.0	23.0	0.60
MID-2	4444	165	309	73.2	0.82	0.03	0.82	14.2	13.0	2.6	1.3	0.26	13.1	69	123.5	91.3	26.0	0.56
MID-2	4444	166	293	96.5	0.43	0.10	0.79	12.8	12.5	2.5	0.3	0.26	12.0	64	113.2	66.7	19.0	0.56
MID-2	4444	167	303	89.8	0.52	0.13	0.82	13.5	12.5	2.6	1.0	0.21	12.7	61	91.0	75.9	20.0	0.52
MID-2	4444	168	297	103.8	0.55	0.09	0.81	14.4	12.8	2.8	1.6	0.26	12.6	66	119.3	75.5	23.0	0.39
MID-2	4442	501	174	66.8	0.46	0.13	0.55	9.0	8.5	1.8	0.5	0.15	8.4	80	98.9	70.4	21.0	0.80
MID-2	4442	502	185	74.5	0.31	0.15	0.54	9.4	8.8	1.9	0.6	0.14	8.7	71	97.4	57.5	21.0	0.80
MID-2	4442	503	196	50.9	0.32	0.21	0.60	9.7	9.1	2.0	0.6	0.19	9.5	76	102.6	72.3	24.0	0.78
MID-2	4442	504	181	59.9	0.38	0.18	0.59	10.1	[illegible]	2.4	1.2	0.19	8.9	82	103.6	80.5	25.0	0.80
MID-2	4442	505	195	80.8	0.31	0.19	0.63	9.9	9.1	1.8	0.7	0.19	9.1	71	91.8	63.8	22.0	0.80
MID-2	4442	506	182	95.9	0.39	0.16	0.90	14.2	13.1	2.8	1.1	0.17	12.7	77	133.7	103.5	27.0	0.63
MID-2	4442	507	184	81.3	0.32	0.29	0.66	10.4	9.7	1.8	0.7	0.16	9.1	75	89.6	69.4	21.0	0.62
MID-2	4442	508	184	65.1	0.39	0.21	0.48	9.3	8.1	2.8	1.2	0.19	8.5	76	102.1	66.9	21.0	0.86
MID-2	4444	561	181	92.1	0.45	0.14	0.94	15.9	14.3	3.7	1.6	0.15	14.0	72	134.4	97.9	25.0	0.95
MID-2	4444	562	186	82.3	0.49	0.09	1.00	16.1	14.8	2.9	1.3	0.14	14.7	66	138.0	85.5	32.0	0.60
MID-2	4444	563	177	99.9	0.53	0.06	0.67	10.2	9.7	1.9	0.6	0.20	9.3	76	105.3	73.2	23.0	0.64
MID-2	4444	564	190	64.5	0.52	0.14	0.59	10.5	9.5	2.2	1.0	0.18	9.8	75	93.2	76.8	25.0	0.82

TIME	EXPT	ANIMAL	GRAMS	MV	CDYN	RL	CCORD	TLC	VC	FRC	RV	DLCO	FVC	FEV1	PEFR	MMEF	EF10	SIII
MID-2	4444	565	182	119.6	0.48	0.10	0.93	15.3	14.2	3.3	1.1	0.21	14.0	73	139.6	106.6	31.0	0.83
MID-2	4444	566	183	48.7	0.41	0.14	0.56	9.2	8.9	1.4	0.3	0.14	8.6	77	92.6	70.0	14.0	0.70
MID-2	4444	567	184	65.4	0.25	0.19	0.71	10.5	9.5	2.2	1.0	0.18	9.6	73	99.5	68.7	21.0	0.62
MID-2	4444	568	187	66.7	0.53	0.14	0.64	10.0	9.1	2.1	0.9	0.18	9.4	78	93.1	78.8	23.0	0.89
EOE-2	4442	101	303	78.3	0.45	0.15	0.73	14.0	12.4	2.6	1.6	0.27	11.9	68	115.5	76.5	18.0	0.63
EOE-2	4442	102	331	79.2	0.65	0.10	0.75	12.2	11.4	2.7	0.8	0.25	10.9	75	107.9	85.8	27.0	0.77
EOE-2	4442	103	314	72.3	0.44	0.17	0.72	11.7	11.4	1.8	0.3	0.25	10.7	71	107.7	72.6	27.0	0.61
EOE-2	4442	104	328	90.8	0.34	0.14	0.83	13.1	12.1	2.2	1.0	0.32	11.5	70	116.0	78.3	25.0	0.53
EOE-2	4442	105	319	79.8	0.56	0.07	0.70	13.4	12.4	2.2	1.0	0.31	12.1	67	116.8	74.1	23.0	0.63
EOE-2	4442	106	340	78.4	0.43	0.09	0.65	11.8	11.0	2.1	0.8	0.33	11.3	60	89.6	57.7	20.0	0.88
EOE-2	4442	107	333	68.3	0.37	0.12	0.64	12.2	11.0	2.5	1.2	0.30	10.6	70	95.2	74.1	20.0	0.36
EOE-2	4442	108	344	76.4	0.60	0.11	0.91	14.2	12.6	2.8	1.6	0.32	12.7	59	117.6	56.3	20.0	1.03
EOE-2	4444	161	317	64.3	0.56	0.10	0.63	10.8	10.4	1.8	0.4	0.29	10.4	70	105.8	68.7	20.0	1.22
EOE-2	4444	162	313	84.0	0.56	0.15	0.70	11.9	10.5	2.1	1.4	0.27	10.5	71	102.3	73.5	17.0	0.42
EOE-2	4444	163	337	78.9	0.42	0.17	0.77	13.0	11.7	2.4	1.3	0.28	11.5	69	100.7	82.9	23.0	1.02
EOE-2	4444	164	333	96.6	0.35	0.14	0.74	13.8	12.4	2.9	1.4	0.34	12.2	68	116.4	78.3	22.0	0.57
EOE-2	4444	165	325	71.2	0.52	0.12	0.75	12.6	11.3	2.6	1.3	0.27	12.1	67	117.7	76.0	24.0	0.59
EOE-2	4444	166	314	68.7	0.36	0.18	0.78	12.8	12.0	2.3	0.8	0.30	12.3	67	103.6	81.4	26.0	0.68
EOE-2	4444	167	324	78.9	0.42	0.22	0.74	11.1	10.9	2.1	0.2	0.29	11.5	66	91.5	74.0	22.0	0.59
EOE-2	4444	168	329	86.0	0.39	0.16	0.78	13.5	12.3	2.6	1.3	0.27	11.9	68	114.2	79.0	21.0	0.80
EOE-2	4442	501	188	68.6	0.39	0.17	0.58	9.4	8.6	2.0	0.7	0.21	8.9	79	96.2	72.1	23.0	0.81
EOE-2	4442	502	193	74.9	0.32	0.19	0.59	9.1	8.8	1.5	0.3	0.19	8.7	76	86.5	68.4	19.0	0.90
EOE-2	4442	503	208	86.7	0.47	0.14	0.69	10.3	10.1	1.8	0.2	0.23	9.4	77	99.7	76.7	23.0	0.43
EOE-2	4442	504	191	70.5	0.34	0.17	0.68	10.2	9.4	2.1	0.7	0.21	9.4	78	97.4	79.0	22.0	0.66
EOE-2	4442	505	206	56.1	0.24	0.22	0.67	13.1	10.5	3.9	2.6	0.21	10.3	77	109.2	84.1	22.0	0.47
EOE-2	4442	506	193	71.1	0.32	0.18	0.54	9.1	8.1	1.8	1.0	0.17	7.6	85	93.1	74.4	19.0	1.15
EOE-2	4442	507	200	72.7	0.39	0.15	0.65	10.4	9.5	2.2	0.9	0.20	9.5	75	99.5	72.4	22.0	0.58
EOE-2	4442	508	197	58.4	0.23	0.22	0.57	8.9	8.3	1.7	0.6	0.20	8.2	82	97.1	77.0	18.0	0.76
EOE-2	4444	561	201	63.6	0.28	0.22	0.61	10.4	10.0	1.9	0.4	0.19	9.1	79	103.8	79.2	19.0	0.58
EOE-2	4444	562	200	60.3	0.51	0.24	0.61	9.7	9.2	1.9	0.5	0.22	8.2	41	72.8	8.0	3.0	0.91
EOE-2	4444	563	189	84.5	0.32	0.19	0.68	10.4	9.4	2.1	0.9	0.22	9.4	79	107.7	79.3	22.0	0.58
EOE-2	4444	564	204	66.4	0.38	0.16	0.67	11.5	10.4	2.3	1.1	0.22	10.3	76	112.0	80.8	27.0	0.55
EOE-2	4444	565	190	62.3	0.31	0.14	0.58	8.7	8.5	1.5	0.2	0.21	8.5	73	89.4	61.3	20.0	0.46
EOE-2	4444	566	199	57.9	0.28	0.17	0.59	9.8	8.9	1.8	0.9	0.18	8.7	72	92.2	58.8	20.0	0.58
EOE-2	4444	567	200	40.3	0.28	0.20	0.65	10.5	9.3	2.0	1.1	0.16	9.3	68	100.7	58.6	22.0	0.83
EOE-2	4444	568	198	75.4	0.32	0.31	0.63	9.9	9.4	1.9	0.5	0.19	9.1	77	88.0	74.3	24.0	0.76
REC-2	4442	101	339	75.5	0.32	0.17	0.79	12.6	11.8	2.6	0.8	0.26	11.6	69	110.8	74.5	26.0	0.35
REC-2	4442	102	355	73.3	0.74	0.07	0.78	11.7	11.3	1.9	0.4	0.31	11.4	69	104.8	77.1	27.0	0.86
REC-2	4442	103	341	94.9	0.33	0.14	0.81	13.2	12.3	2.3	0.9	0.24	12.0	70	110.9	86.4	26.0	0.85
REC-2	4442	104	361	96.3	0.46	0.12	0.85	13.6	12.5	2.8	1.1	0.28	12.0	67	117.6	75.4	21.0	0.67
REC-2	4442	105	347	70.3	0.34	0.25	0.75	11.6	11.3	2.2	0.3	0.31	11.7	63	97.2	66.6	18.0	0.46

TIME	EXPT	ANIMAL	GRAMS	MV	CDYN	RL	CCORD	TLC	VC	FRC	RV	DLCO	FVC	FEV1	PEFR	MMEF	EF10	SIII
REC-2	4442	106	371	74.6	0.41	0.15	0.63	12.1	11.0	2.1	1.0	0.30	11.4	63	97.1	63.3	25.0	0.81
REC-2	4442	107	375	60.7	0.40	0.10	0.72	11.5	11.2	1.6	0.3	0.34	10.8	71	93.5	77.6	20.0	0.82
REC-2	4442	108	322	79.3	0.54	0.14	0.58	12.7	11.4	2.4	1.3	0.28	11.6	63	108.0	63.1	24.0	0.50
REC-2	4444	161	336	78.8	0.44	0.16	0.75	12.3	11.4	2.5	0.9	0.30	11.7	70	110.0	81.5	24.0	0.68
REC-2	4444	162	337	89.3	0.45	0.13	0.73	12.9	11.5	2.4	1.4	0.27	11.2	74	116.2	82.8	21.0	0.66
REC-2	4444	163	358	81.2	0.38	0.13	0.74	13.0	11.5	2.5	1.5	0.29	12.0	69	112.6	77.1	22.0	0.89
REC-2	4444	164	366	90.5	0.66	0.09	0.77	13.2	12.1	2.7	1.1	0.30	12.4	69	116.9	84.4	24.0	0.57
REC-2	4444	165	358	77.8	0.45	0.10	0.82	13.6	12.4	2.4	1.2	0.28	12.6	70	117.7	90.3	26.0	0.74
REC-2	4444	166	346	81.1	0.55	0.10	0.71	14.5	12.5	3.5	2.1	0.30	12.5	61	106.7	63.8	17.0	0.54
REC-2	4444	167	347	102.0	0.44	0.20	0.73	12.9	12.0	2.8	0.9	0.28	12.0	64	99.4	68.4	17.0	0.70
REC-2	4444	168	349	100.4	0.59	0.07	0.80	14.2	12.8	3.1	1.4	0.26	12.8	68	112.8	89.0	25.0	0.65
REC-2	4442	501	194	74.1	0.49	0.15	0.64	10.4	9.2	2.2	1.1	0.20	8.3	63	74.9	44.1	11.0	0.55
REC-2	4442	502	202	93.3	0.29	0.20	0.65	10.0	9.1	1.9	0.9	0.17	9.0	49	60.5	26.1	4.0	0.67
REC-2	4442	503	221	105.5	0.37	0.17	0.69	10.4	10.1	2.3	0.2	0.23	10.2	76	102.8	85.9	26.0	0.49
REC-2	4442	504	201	53.2	0.29	0.17	0.54	9.3	8.5	2.1	0.7	0.17	8.2	82	97.0	77.4	21.0	0.57
REC-2	4442	505	208	73.4	0.30	0.18	0.69	11.5	10.3	2.5	1.2	0.19	9.7	47	72.1	25.7	9.0	0.85
REC-2	4442	506	188	73.2	0.25	0.27	0.58	8.8	8.3	1.4	0.5	0.16	8.2	75	81.2	64.6	18.0	0.68
REC-2	4442	507	210	70.8	0.30	0.19	0.60	9.6	8.7	1.6	0.9	0.21	8.5	79	100.8	69.4	19.0	0.39
REC-2	4442	508	208	81.6	0.41	0.17	0.62	9.6	8.8	1.6	0.8	0.21	8.6	79	91.6	75.1	19.0	0.88
REC-2	4444	561	208	93.3	0.29	0.20	0.65	10.4	9.1	2.2	1.3	0.21	10.6	44	76.8	20.1	6.0	0.48
REC-2	4444	562	201	73.7	0.29	0.22	0.60	9.7	9.4	1.8	0.3	0.18	8.3	63	74.9	44.1	11.0	0.77
REC-2	4444	563	194	90.4	0.47	0.17	0.66	11.5	10.5	2.4	1.0	0.20	10.2	70	99.1	71.3	22.0	0.56
REC-2	4444	564	211	60.4	0.36	0.22	0.76	11.6	10.9	2.1	0.8	0.21	10.6	58	89.4	42.7	13.0	0.51
REC-2	4444	565	201	64.2	0.33	0.25	0.50	7.8	7.5	1.2	0.3	0.25	8.1	76	80.3	64.2	19.0	0.77
REC-2	4444	566	208	67.1	0.49	0.18	0.67	10.3	9.6	1.9	0.7	0.21	9.1	78	102.0	76.7	24.0	0.86
REC-2	4444	567	211	77.1	0.39	0.46	0.63	10.2	9.9	1.9	0.3	0.20	9.5	38	70.6	9.7	3.0	0.43
REC-2	4444	568	201	58.9	0.26	0.28	0.63	9.6	8.9	2.0	0.7	0.17	9.0	76	96.5	70.9	18.0	0.88

NOTE: Time codes are defined as BASE = base level evaluations made prior to exposure; MID = evaluations made mid-way through the 13-week exposure; EOE = evaluations made after the last exposure; and REC = evaluations made after the 4-week recovery period. The code with -1 and -2 indicate evaluations relate to Phase III, Part 1 or Phase III, Part 2, respectively.

APPENDIX H: GROUP SUMMARIES OF HISTOPATHOLOGY OBSERVATIONS

EXPT NUMBER	CONCENTRATION OF Cu-Zn	EAR TAG	ANIMAL NUMBER	ANIMAL SEX	SACRIFICE CODE	RESPIRATORY TRACT LESION CATEGORY AND SEVERITY OF LESION: NASAL EPITHELIAL ATROPHY	ALVEOLAR MACROPHAGE HYPERPLASIA	TYPE II PNEUMOCYTE HYPERPLASIA	ALVEOLITIS	NASAL GOBLET CELL HYPERPLASIA
4371	1.0 mg/m3	Q	037	MALE	EOE	0	0	0	0	0
4371	1.0 mg/m3	Q	038	MALE	EOE	0	0	0	0	0
4371	1.0 mg/m3	Q	040	MALE	REC	0	0	0	0	0
4371	1.0 mg/m3	Q	043	MALE	EOE	0	0	0	0	0
4371	1.0 mg/m3	Q	044	MALE	EOE	0	0	0	0	0
4371	1.0 mg/m3	Q	046	MALE	EOE	0	0	0	0	0
4371	1.0 mg/m3	Q	048	MALE	REC	0	0	1	0	0
4371	1.0 mg/m3	Q	049	MALE	EOE	0	0	0	0	0
4371	1.0 mg/m3	Q	050	MALE	REC	0	0	0	0	0
4371	1.0 mg/m3	Q	051	MALE	REC	0	0	0	0	0
4371	1.0 mg/m3	Q	052	MALE	EOE	0	0	0	0	0
4371	1.0 mg/m3	Q	055	MALE	REC	0	0	0	0	0
4371	1.0 mg/m3	Q	056	MALE	REC	0	0	0	0	0
4371	1.0 mg/m3	Q	059	MALE	EOE	1	0	0	0	0
4371	1.0 mg/m3	Q	060	MALE	REC	0	0	0	0	0
4371	1.0 mg/m3	Q	061	MALE	EOE	0	0	0	0	0
4371	1.0 mg/m3	Q	062	MALE	REC	0	0	0	0	0
4371	1.0 mg/m3	Q	063	MALE	EOE	0	0	0	0	0
4371	1.0 mg/m3	Q	066	MALE	REC	0	0	0	0	0
4371	1.0 mg/m3	Q	067	MALE	REC	0	0	0	0	0
4371	1.0 mg/m3	Q	070	MALE	REC	0	0	0	0	0
4371	1.0 mg/m3	Q	072	MALE	EOE	1	0	0	0	0
4371	1.0 mg/m3	Q	537	FEMALE	EOE	1	0	0	0	0
4371	1.0 mg/m3	Q	540	FEMALE	REC	0	0	0	0	0
4371	1.0 mg/m3	Q	541	FEMALE	REC	0	0	0	0	0
4371	1.0 mg/m3	Q	543	FEMALE	EOE	0	0	0	0	0
4371	1.0 mg/m3	Q	544	FEMALE	REC	0	0	0	0	0
4371	1.0 mg/m3	Q	547	FEMALE	EOE	0	0	0	0	0
4371	1.0 mg/m3	Q	548	FEMALE	EOE	0	0	0	0	0
4371	1.0 mg/m3	Q	549	FEMALE	EOE	0	0	0	0	0
4371	1.0 mg/m3	Q	550	FEMALE	REC	0	0	0	0	0
4371	1.0 mg/m3	Q	554	FEMALE	EOE	0	0	0	0	0
4371	1.0 mg/m3	Q	555	FEMALE	REC	0	0	0	0	0
4371	1.0 mg/m3	Q	556	FEMALE	REC	0	0	0	0	0

EXPT NUMBER	CONCENTRATION OF Cu-Zn	EAR TAG	ANIMAL NUMBER	ANIMAL SEX	SACRIFICE CODE	RESPIRATORY TRACT LESION CATEGORY AND SEVERITY OF LESION: NASAL EPITHELIAL ATROPHY	ALVEOLAR MACROPHAGE HYPERPLASIA	TYPE II PNEUMOCYTE HYPERPLASIA	ALVEOLITIS	NASAL GOBLET CELL HYPERPLASIA
4371	1.0 mg/m3	Q	558	FEMALE	REC	0	0	0	0	0
4371	1.0 mg/m3	Q	560	FEMALE	REC	0	0	0	0	0
4371	1.0 mg/m3	Q	562	FEMALE	REC	0	0	0	0	0
4371	1.0 mg/m3	Q	563	FEMALE	REC	0	0	0	0	0
4371	1.0 mg/m3	Q	564	FEMALE	EOE	0	0	0	0	0
4371	1.0 mg/m3	Q	566	FEMALE	REC	0	0	0	0	0
4371	1.0 mg/m3	Q	567	FEMALE	EOE	0	0	0	0	0
4371	1.0 mg/m3	Q	569	FEMALE	EOE	0	0	0	0	0
4371	1.0 mg/m3	Q	570	FEMALE	EOE	0	0	0	0	0
4371	1.0 mg/m3	Q	571	FEMALE	EOE	0	0	0	0	0
4372	3.2 mg/m3	Q	075	MALE	EOE	0	1	1	1	0
4372	3.2 mg/m3	Q	076	MALE	REC	0	0	0	0	0
4372	3.2 mg/m3	Q	079	MALE	REC	0	1	1	0	0
4372	3.2 mg/m3	Q	080	MALE	EOE	0	1	1	0	0
4372	3.2 mg/m3	Q	081	MALE	EOE	1	0	0	0	0
4372	3.2 mg/m3	Q	085	MALE	EOE	0	0	0	0	0
4372	3.2 mg/m3	Q	086	MALE	REC	1	0	0	0	0
4372	3.2 mg/m3	Q	087	MALE	EOE	0	1	0	0	0
4372	3.2 mg/m3	Q	090	MALE	EOE	1	1	1	1	0
4372	3.2 mg/m3	Q	092	MALE	REC	0	0	0	0	0
4372	3.2 mg/m3	Q	093	MALE	REC	0	0	0	0	0
4372	3.2 mg/m3	Q	095	MALE	REC	0	1	0	0	0
4372	3.2 mg/m3	Q	096	MALE	REC	0	0	0	0	0
4372	3.2 mg/m3	Q	100	MALE	EOE	0	1	1	1	0
4372	3.2 mg/m3	Q	101	MALE	EOE	0	0	0	0	0
4372	3.2 mg/m3	Q	102	MALE	REC	0	1	1	0	0
4372	3.2 mg/m3	Q	103	MALE	EOE	0	1	0	0	0
4372	3.2 mg/m3	Q	104	MALE	EOE	0	0	0	0	0
4372	3.2 mg/m3	Q	109	MALE	EOE	0	1	1	1	0
4372	3.2 mg/m3	Q	111	MALE	REC	0	0	0	0	0
4372	3.2 mg/m3	Q	112	MALE	REC	0	0	0	0	0
4372	3.2 mg/m3	Q	575	FEMALE	EOE	0	1	0	0	0
4372	3.2 mg/m3	Q	576	FEMALE	REC	0	1	1	0	0
4372	3.2 mg/m3	Q	578	FEMALE	REC	0	0	0	0	0
4372	3.2 mg/m3	Q	579	FEMALE	REC	0	0	0	0	0
4372	3.2 mg/m3	Q	580	FEMALE	EOE	0	0	0	0	0
4372	3.2 mg/m3	Q	584	FEMALE	REC	0	0	0	0	0

EXPT NUMBER	CONCENTRATION OF Cu-Zn	EAR TAG	ANIMAL NUMBER	ANIMAL SEX	SACRIFICE CODE	RESPIRATORY TRACT LESION CATEGORY AND SEVERITY OF LESION				
						NASAL EPITHELIAL ATROPHY	ALVEOLAR MACROPHAGE HYPERPLASIA	TYPE II PNEUMOCYTE HYPERPLASIA	ALVEOLITIS	NASAL GOBLET CELL HYPERPLASIA
4372	3.2 mg/m3	Q	585	FEMALE	REC	0	1	1	0	0
4372	3.2 mg/m3	Q	588	FEMALE	EOE	0	1	0	0	0
4372	3.2 mg/m3	Q	590	FEMALE	EOE	0	1	0	1	0
4372	3.2 mg/m3	Q	591	FEMALE	REC	0	0	0	0	0
4372	3.2 mg/m3	Q	592	FEMALE	EOE	0	0	0	0	0
4372	3.2 mg/m3	Q	593	FEMALE	EOE	0	0	0	0	0
4372	3.2 mg/m3	Q	598	FEMALE	REC	0	0	0	0	0
4372	3.2 mg/m3	Q	599	FEMALE	EOE	0	1	1	1	0
4372	3.2 mg/m3	Q	600	FEMALE	REC	0	0	0	0	0
4372	3.2 mg/m3	Q	602	FEMALE	REC	0	0	0	0	0
4372	3.2 mg/m3	Q	603	FEMALE	EOE	1	1	1	1	0
4372	3.2 mg/m3	Q	604	FEMALE	REC	0	0	0	0	0
4372	3.2 mg/m3	Q	605	FEMALE	EOE	0	1	0	0	0
4372	3.2 mg/m3	Q	606	FEMALE	REC	0	0	0	0	0
4372	3.2 mg/m3	Q	608	FEMALE	EOE	0	0	0	0	0
4372	3.2 mg/m3	Q	609	FEMALE	EOE	0	1	0	0	0
4373	10 mg/m3	Q	114	MALE	EOE	1	2	1	2	0
4373	10 mg/m3	Q	116	MALE	REC	1	1	1	0	0
4373	10 mg/m3	Q	117	MALE	REC	2	1	1	0	0
4373	10 mg/m3	Q	119	MALE	REC	0	1	1	0	0
4373	10 mg/m3	Q	122	MALE	REC	0	1	1	0	0
4373	10 mg/m3	Q	125	MALE	EOE	1	0	0	0	0
4373	10 mg/m3	Q	126	MALE	EOE	2	0	0	0	0
4373	10 mg/m3	Q	127	MALE	REC	0	1	1	0	0
4373	10 mg/m3	Q	128	MALE	EOE	1	1	1	1	0
4373	10 mg/m3	Q	130	MALE	EOE	1	1	1	1	0
4373	10 mg/m3	Q	132	MALE	EOE	1	1	1	1	0
4373	10 mg/m3	Q	133	MALE	EOE	1	1	1	1	0
4373	10 mg/m3	Q	134	MALE	REC	0	1	1	0	0
4373	10 mg/m3	Q	135	MALE	REC	1	2	2	0	0
4373	10 mg/m3	Q	136	MALE	EOE	1	2	2	2	0
4373	10 mg/m3	Q	140	MALE	EOE	0	1	1	1	0
4373	10 mg/m3	Q	141	MALE	EOE	2	2	2	2	0
4373	10 mg/m3	Q	142	MALE	EOE	2	2	1	2	0
4373	10 mg/m3	Q	144	MALE	REC	0	1	1	0	0
4373	10 mg/m3	Q	147	MALE	REC	1	1	1	0	0
4373	10 mg/m3	Q	148	MALE	REC	0	1	1	0	0

EXPT NUMBER	CONCENTRATION OF Cu-Zn	EAR TAG	ANIMAL NUMBER	ANIMAL SEX	SACRIFICE CODE	RESPIRATORY TRACT LESION CATEGORY AND SEVERITY OF LESION				
						NASAL EPITHELIAL ATROPHY	ALVEOLAR MACROPHAGE HYPERPLASIA	TYPE II PNEUMOCYTE HYPERPLASIA	ALVEOLITIS	NASAL GOBLET CELL HYPERPLASIA
4373	10 mg/m3	Q	149	MALE	REC	0	1	1	0	0
4373	10 mg/m3	Q	615	FEMALE	EOE	1	2	2	2	0
4373	10 mg/m3	Q	616	FEMALE	REC	0	1	1	0	0
4373	10 mg/m3	Q	617	FEMALE	EOE	1	2	1	2	0
4373	10 mg/m3	Q	618	FEMALE	REC	0	1	1	0	0
4373	10 mg/m3	Q	620	FEMALE	EOE	0	2	1	2	0
4373	10 mg/m3	Q	624	FEMALE	REC	1	1	1	0	0
4373	10 mg/m3	Q	625	FEMALE	EOE	0	1	1	1	0
4373	10 mg/m3	Q	626	FEMALE	REC	0	1	1	0	0
4373	10 mg/m3	Q	627	FEMALE	REC	0	1	1	0	0
4373	10 mg/m3	Q	628	FEMALE	EOE	1	1	1	1	0
4373	10 mg/m3	Q	630	FEMALE	EOE	0	1	1	1	0
4373	10 mg/m3	Q	631	FEMALE	REC	0	1	1	0	0
4373	10 mg/m3	Q	632	FEMALE	EOE	0	1	1	1	0
4373	10 mg/m3	Q	633	FEMALE	EOE	1	1	1	1	0
4373	10 mg/m3	Q	634	FEMALE	REC	1	1	1	0	0
4373	10 mg/m3	Q	636	FEMALE	EOE	1	0	0	0	0
4373	10 mg/m3	Q	638	FEMALE	EOE	0	0	0	0	0
4373	10 mg/m3	Q	639	FEMALE	REC	1	1	1	0	0
4373	10 mg/m3	Q	642	FEMALE	REC	0	1	1	0	0
4373	10 mg/m3	Q	643	FEMALE	EOE	0	1	0	1	0
4373	10 mg/m3	Q	648	FEMALE	REC	0	1	1	0	0
4373	10 mg/m3	Q	650	FEMALE	REC	0	1	1	0	0
4442	0 (SHAM)	G	109	MALE	REC	0	0	0	0	0
4442	0 (SHAM)	G	110	MALE	REC	0	0	0	0	0
4442	0 (SHAM)	G	111	MALE	EOE	0	0	0	0	0
4442	0 (SHAM)	G	112	MALE	EOE	0	0	0	0	0
4442	0 (SHAM)	G	114	MALE	REC	0	0	0	0	0
4442	0 (SHAM)	G	115	MALE	EOE	0	0	0	0	0
4442	0 (SHAM)	G	116	MALE	EOE	0	0	0	0	0
4442	0 (SHAM)	G	118	MALE	REC	0	0	0	0	0
4442	0 (SHAM)	G	119	MALE	EOE	0	0	0	0	0
4442	0 (SHAM)	G	120	MALE	EOE	0	0	0	0	0
4442	0 (SHAM)	G	121	MALE	REC	0	0	0	0	0
4442	0 (SHAM)	G	122	MALE	EOE	0	0	0	0	0
4442	0 (SHAM)	G	123	MALE	REC	0	0	0	0	0
4442	0 (SHAM)	G	127	MALE	EOE	0	0	0	0	0

EXPT NUMBER	CONCENTRATION OF Cu-Zn	EAR TAG	ANIMAL NUMBER	ANIMAL SEX	SACRIFICE CODE	RESPIRATORY TRACT LESION CATEGORY AND SEVERITY OF LESION				
						NASAL EPITHELIAL ATROPHY	ALVEOLAR MACROPHAGE HYPERPLASIA	TYPE II PNEUMOCYTE HYPERPLASIA	ALVEOLITIS	NASAL GOBLET CELL HYPERPLASIA
4442	0 (SHAM)	G	128	MALE	EOE	0	0	0	0	0
4442	0 (SHAM)	G	130	MALE	REC	0	0	0	0	0
4442	0 (SHAM)	G	131	MALE	REC	0	0	0	0	0
4442	0 (SHAM)	G	132	MALE	REC	0	0	0	0	0
4442	0 (SHAM)	G	134	MALE	REC	0	0	0	0	0
4442	0 (SHAM)	G	136	MALE	EOE	0	0	0	0	0
4442	0 (SHAM)	G	137	MALE	REC	0	0	0	0	0
4442	0 (SHAM)	G	138	MALE	EOE	0	0	0	0	0
4442	0 (SHAM)	G	509	FEMALE	EOE	0	0	0	0	0
4442	0 (SHAM)	G	510	FEMALE	REC	0	0	0	0	0
4442	0 (SHAM)	G	511	FEMALE	REC	0	1	0	0	0
4442	0 (SHAM)	G	512	FEMALE	REC	0	0	0	0	0
4442	0 (SHAM)	G	513	FEMALE	REC	0	0	0	0	0
4442	0 (SHAM)	G	515	FEMALE	REC	0	0	0	0	0
4442	0 (SHAM)	G	516	FEMALE	REC	0	0	0	0	0
4442	0 (SHAM)	G	517	FEMALE	EOE	0	1	0	0	0
4442	0 (SHAM)	G	518	FEMALE	REC	0	0	0	0	0
4442	0 (SHAM)	G	519	FEMALE	EOE	0	0	0	0	0
4442	0 (SHAM)	G	520	FEMALE	EOE	0	0	0	0	0
4442	0 (SHAM)	G	522	FEMALE	REC	0	1	0	0	0
4442	0 (SHAM)	G	523	FEMALE	REC	0	0	0	0	0
4442	0 (SHAM)	G	524	FEMALE	EOE	0	0	0	0	0
4442	0 (SHAM)	G	526	FEMALE	EOE	0	0	0	0	0
4442	0 (SHAM)	G	527	FEMALE	EOE	0	0	0	0	0
4442	0 (SHAM)	G	530	FEMALE	REC	0	1	0	0	0
4442	0 (SHAM)	G	531	FEMALE	EOE	0	0	0	0	0
4442	0 (SHAM)	G	532	FEMALE	EOE	0	0	0	0	0
4442	0 (SHAM)	G	533	FEMALE	EOE	0	0	0	0	0
4442	0 (SHAM)	G	535	FEMALE	REC	0	0	0	0	0
4442	0 (SHAM)	G	538	FEMALE	EOE	0	0	0	0	0
4443	0.32 mg/m3	G	139	MALE	REC	0	0	0	0	0
4443	0.32 mg/m3	G	140	MALE	REC	0	0	0	0	0
4443	0.32 mg/m3	G	141	MALE	EOE	0	0	0	0	0
4443	0.32 mg/m3	G	142	MALE	REC	0	0	0	0	0
4443	0.32 mg/m3	G	143	MALE	REC	0	0	0	0	0
4443	0.32 mg/m3	G	144	MALE	EOE	0	0	0	0	0
4443	0.32 mg/m3	G	145	MALE	EOE	0	0	0	0	0

EXPT NUMBER	CONCENTRATION OF Cu-Zn	EAR TAG	ANIMAL NUMBER	ANIMAL SEX	SACRIFICE CODE	NASAL EPITHELIAL ATROPHY	ALVEOLAR MACROPHAGE HYPERPLASIA	TYPE II PNEUMOCYTE HYPERPLASIA	ALVEOLITIS	NASAL GOBLET CELL HYPERPLASIA
						RESPIRATORY TRACT LESION CATEGORY AND SEVERITY OF LESION				
4443	0.32 mg/m3	G	146	MALE	EOE	0	0	0	0	0
4443	0.32 mg/m3	G	147	MALE	REC	0	0	0	0	0
4443	0.32 mg/m3	G	148	MALE	EOE	0	0	0	0	0
4443	0.32 mg/m3	G	149	MALE	EOE	0	0	0	0	0
4443	0.32 mg/m3	G	150	MALE	REC	0	0	0	0	0
4443	0.32 mg/m3	G	151	MALE	REC	0	0	0	0	0
4443	0.32 mg/m3	G	152	MALE	REC	0	0	0	0	0
4443	0.32 mg/m3	G	153	MALE	EOE	0	0	0	0	0
4443	0.32 mg/m3	G	154	MALE	EOE	0	0	0	0	0
4443	0.32 mg/m3	G	155	MALE	REC	0	0	0	0	0
4443	0.32 mg/m3	G	156	MALE	EOE	0	0	0	0	0
4443	0.32 mg/m3	G	157	MALE	EOE	0	0	0	0	0
4443	0.32 mg/m3	G	158	MALE	REC	0	0	0	0	0
4443	0.32 mg/m3	G	159	MALE	EOE	0	0	0	0	0
4443	0.32 mg/m3	G	160	MALE	REC	0	0	0	0	0
4443	0.32 mg/m3	G	539	FEMALE	REC	0	0	0	0	0
4443	0.32 mg/m3	G	540	FEMALE	EOE	0	0	0	0	0
4443	0.32 mg/m3	G	541	FEMALE	REC	0	0	0	0	0
4443	0.32 mg/m3	G	542	FEMALE	EOE	0	0	0	0	0
4443	0.32 mg/m3	G	543	FEMALE	REC	0	0	0	0	0
4443	0.32 mg/m3	G	544	FEMALE	EOE	0	0	0	0	0
4443	0.32 mg/m3	G	545	FEMALE	REC	0	0	0	0	0
4443	0.32 mg/m3	G	546	FEMALE	EOE	0	0	0	0	0
4443	0.32 mg/m3	G	547	FEMALE	EOE	0	0	0	0	0
4443	0.32 mg/m3	G	548	FEMALE	REC	0	0	0	0	0
4443	0.32 mg/m3	G	549	FEMALE	EOE	0	0	0	0	0
4443	0.32 mg/m3	G	550	FEMALE	REC	0	0	0	0	0
4443	0.32 mg/m3	G	551	FEMALE	EOE	0	0	0	0	0
4443	0.32 mg/m3	G	552	FEMALE	REC	0	0	0	0	0
4443	0.32 mg/m3	G	553	FEMALE	REC	0	1	1	1	0
4443	0.32 mg/m3	G	554	FEMALE	REC	0	0	0	0	0
4443	0.32 mg/m3	G	555	FEMALE	EOE	0	0	0	0	0
4443	0.32 mg/m3	G	556	FEMALE	REC	0	0	0	0	0
4443	0.32 mg/m3	G	557	FEMALE	REC	0	0	0	0	0
4443	0.32 mg/m3	G	558	FEMALE	EOE	0	0	0	0	0
4443	0.32 mg/m3	G	559	FEMALE	EOE	0	0	0	0	0
4443	0.32 mg/m3	G	560	FEMALE	EOE	0	0	0	0	0

EXPT NUMBER	CONCENTRATION OF Cu-Zn	EAR TAG	ANIMAL NUMBER	ANIMAL SEX	SACRIFICE CODE	RESPIRATORY TRACT LESION CATEGORY AND SEVERITY OF LESION				
						NASAL EPITHELIAL ATROPHY	ALVEOLAR MACROPHAGE HYPERPLASIA	TYPE II PNEUMOCYTE HYPERPLASIA	ALVEOLITIS	NASAL GOBLET CELL HYPERPLASIA
4444	3.2 mg/m3	G	170	MALE	REC	0	0	0	0	0
4444	3.2 mg/m3	G	171	MALE	REC	0	0	0	0	0
4444	3.2 mg/m3	G	173	MALE	REC	0	1	0	0	0
4444	3.2 mg/m3	G	174	MALE	REC	0	0	0	0	0
4444	3.2 mg/m3	G	175	MALE	EOE	0	0	0	0	0
4444	3.2 mg/m3	G	177	MALE	REC	0	1	1	1	0
4444	3.2 mg/m3	G	179	MALE	REC	0	0	0	0	0
4444	3.2 mg/m3	G	180	MALE	EOE	0	1	0	0	0
4444	3.2 mg/m3	G	181	MALE	EOE	0	1	1	0	0
4444	3.2 mg/m3	G	182	MALE	EOE	0	0	0	0	0
4444	3.2 mg/m3	G	184	MALE	REC	0	1	1	0	0
4444	3.2 mg/m3	G	185	MALE	EOE	0	1	1	1	0
4444	3.2 mg/m3	G	186	MALE	REC	0	0	0	0	0
4444	3.2 mg/m3	G	187	MALE	EOE	0	0	0	0	0
4444	3.2 mg/m3	G	188	MALE	REC	0	0	0	0	0
4444	3.2 mg/m3	G	189	MALE	EOE	1	0	0	0	0
4444	3.2 mg/m3	G	190	MALE	EOE	0	1	1	1	0
4444	3.2 mg/m3	G	191	MALE	EOE	1	1	1	1	0
4444	3.2 mg/m3	G	192	MALE	EOE	1	1	0	0	0
4444	3.2 mg/m3	G	195	MALE	REC	0	0	0	0	0
4444	3.2 mg/m3	G	196	MALE	REC	0	0	0	0	0
4444	3.2 mg/m3	G	197	MALE	EOE	0	1	0	1	0
4444	3.2 mg/m3	G	569	FEMALE	REC	0	0	0	0	0
4444	3.2 mg/m3	G	570	FEMALE	REC	0	1	1	0	0
4444	3.2 mg/m3	G	573	FEMALE	EOE	0	0	0	0	0
4444	3.2 mg/m3	G	574	FEMALE	EOE	0	1	0	0	0
4444	3.2 mg/m3	G	575	FEMALE	REC	0	1	1	0	0
4444	3.2 mg/m3	G	576	FEMALE	REC	0	0	0	0	0
4444	3.2 mg/m3	G	577	FEMALE	REC	0	0	0	0	0
4444	3.2 mg/m3	G	578	FEMALE	EOE	0	0	0	0	0
4444	3.2 mg/m3	G	580	FEMALE	REC	0	0	0	0	0
4444	3.2 mg/m3	G	581	FEMALE	EOE	0	0	0	0	0
4444	3.2 mg/m3	G	582	FEMALE	REC	0	0	0	0	0
4444	3.2 mg/m3	G	583	FEMALE	EOE	0	0	0	0	0
4444	3.2 mg/m3	G	585	FEMALE	REC	0	0	0	0	0
4444	3.2 mg/m3	G	586	FEMALE	EOE	0	0	0	0	0
4444	3.2 mg/m3	G	588	FEMALE	EOE	0	1	0	0	0

EXPT NUMBER	CONCENTRATION OF Cu-Zn	EAR TAG	ANIMAL NUMBER	ANIMAL SEX	SACRIFICE CODE	RESPIRATORY TRACT LESION CATEGORY AND SEVERITY OF LESION				
						NASAL EPITHELIAL ATROPHY	ALVEOLAR MACROPHAGE HYPERPLASIA	TYPE II PNEUMOCYTE HYPERPLASIA	ALVEOLITIS	NASAL GOBLET CELL HYPERPLASIA
4444	3.2 mg/m3	G	589	FEMALE	EOE	0	1	1	0	0
4444	3.2 mg/m3	G	590	FEMALE	EOE	0	0	0	0	0
4444	3.2 mg/m3	G	591	FEMALE	REC	0	0	0	0	0
4444	3.2 mg/m3	G	592	FEMALE	REC	0	0	0	0	0
4444	3.2 mg/m3	G	594	FEMALE	EOE	0	0	0	0	0
4444	3.2 mg/m3	G	595	FEMALE	REC	0	0	0	0	0
4444	3.2 mg/m3	G	596	FEMALE	EOE	0	0	0	0	0

APPENDIX I. SUMMARY TABLES OF ENDPOINT EVALUATIONS AND STATISTICAL COMPARISONS BETWEEN PHASE III, PARTS 1 AND 2 FOR F344/N RATS EXPOSED TO 3.2 mg Cu-Zn ALLOY POWDER/m^3

This appendix presents tabulated data for Phase III, Parts 1 and 2, and a summary table of statistical comparisons between the results for rats exposed to 3.2 mg Cu-Zn in Phase III, Parts 1 and 2. With few exceptions, results were the same for exposures to 3.2 mg Cu-Zn/m^3 in Phase III, Parts 1 and 2. Overall, we felt justified in combining results for the two parts of Phase III wherever possible and comparing all exposed groups of rats with the sham-exposed rats from Phase III, Part 2.

Table I-1

Biochemical Analyses of Bronchoalveolar Lavage Fluid[a] From F344/N Rats That Inhaled Powdered Cu-Zn Alloy

		Aerosol Concentration of Powdered Cu-Zn Alloy, mg/m^3											
		Phase III, Part 1						Phase III, Part 2					
		1.0		3.2		10		0 (Sham)		0.32		3.2	
Lavage Fluid Constituent	Measure	EOE	REC	EOE	REC	EOE	REC	EOE	REC	EOE	REC	EOE	REC
β-Glucuronidase (mIU)	Mean	1.42	1.86	1.84	1.79	7.08	1.36	1.27	1.13	1.62	1.25	1.39	1.11
	SE	0.18	0.31	0.23	0.26	1.11	0.28	0.15	0.13	0.26	0.16	0.22	0.13
	N	12	12	11	12	12	12	12	12	12	12	12	12
Alkaline Phosphatase (mIU)	Mean	411	360	469	293	336	279	285	269	321	284	387	215
	SE	42	51	39	18	38	35	23	21	22	23	38	17
	N	12	12	11	12	12	12	12	12	12	12	12	12
Lactate Dehydrogenase (mIU)	Mean	1124	793	1658	827	2047	839	385	446	389	488	571	406
	SE	186	213	165	144	316	99	32	21	26	38	63	30
	N	12	12	11	12	12	12	12	12	12	12	12	12
Protein (mg)	Mean	1.66	1.16	1.87	1.04	2.82	1.21	1.54	1.55	1.30	1.51	1.54	1.34
	SE	0.09	0.21	0.10	0.14	0.20	0.15	0.09	0.15	0.09	0.21	0.12	0.11
	N	12	12	11	12	12	12	12	12	12	12	12	12

[a]Total amount of β-glucuronidase, alkaline phosphatase, lactate dehydrogenase, and protein in lavage fluid from right lung of F344/N rats in this study.

Table I-2

Total Cells in Lung Lavage Fluid[a]
(Mean ± SE)

Aerosol Concentration of Cu-Zn Alloy	Evaluation Time	
	End of Exposure	After Recovery
Phase III, Part 1		
1.0 mg/m^3	0.88 ± 0.09	1.17 ± 0.08
3.2 mg/m^3	1.44 ± 0.16	1.26 ± 0.14
10.0 mg/m^3	3.15 ± 0.38	0.94 ± 0.11
Phase III, Part 2		
Sham	1.04 ± 0.07	1.04 ± 0.05
0.32 mg/m^3	0.94 ± 0.03	0.95 ± 0.07
3.2 mg/m^3	1.26 ± 0.10	0.89 ± 0.05

[a]The above values show the mean and SE of the total cells counted for the alveolar macrophage phagocytosis assay x 10^6 (N = 12 per group).

Table I-3

Neutrophil Differential in Lung Lavage Fluid[a]
(Mean ± SE)

Aerosol Concentration of Cu-Zn Alloy	Evaluation Time	
	End of Exposure	After Recovery
Phase III, Part 1		
1.0 mg/m^3 (percent)	3.49 ± 0.89	0.75 ± 0.22
(total)	0.032 ± 0.010	0.009 ± 0.003
3.2 mg/m^3 (percent)	4.48 ± 0.70	0.59 ± 0.24
(total)	0.060 ± 0.009	0.007 ± 0.002
10.0 mg/m^3 (percent)	8.79 ± 1.17	0.80 ± 0.34
(total)	0.273 ± 0.044	0.007 ± 0.002
Phase III, Part 2		
Sham (percent)	0.41 ± 0.12	1.01 ± 0.29
(total)	0.004 ± 0.001	0.012 ± 0.004
0.32 mg/m^3 (percent)	0.41 ± 0.14	0.58 ± 0.17
(total)	0.004 ± 0.001	0.006 ± 0.002
3.2 mg/m^3 (percent)	2.03 ± 0.56	0.33 ± 0.11
(total)	0.027 ± 0.008	0.003 ± 0.001

[a]The above values are differentials taken from the lavage of rats used for the alveolar macrophage phagocytosis assay. N = 12 per group and the total numbers are given x 10^6 cells.

Table I-4

Lymphocyte Differential for Lung Lavage Fluid[a]
(Mean ± SE)

Aerosol Concentration of Cu-Zn Alloy	Evaluation Time	
	End of Exposure	After Recovery
Phase III, Part 1		
1.0 mg/m^3 (percent)	5.7 ± 1.0	7.6 ± 1.2
(total)	0.05 ± 0.01	0.09 ± 0.01
3.2 mg/m^3 (percent)	9.2 ± 1.3	12.0 ± 1.4
(total)	0.13 ± 0.02	0.15 ± 0.03
10.0 mg/m^3 (percent)	9.6 ± 1.0	12.7 ± 1.4
(total)	0.30 ± 0.04	0.11 ± 0.01
Phase III, Part 2		
Sham (percent)	9.5 ± 1.8	6.9 ± 0.9
(total)	0.11 ± 0.03	0.07 ± 0.07
0.32 mg/m^3 (percent)	7.1 ± 1.2	7.8 ± 1.4
(total)	0.07 ± 0.01	0.07 ± 0.01
3.2 mg/m^3 (percent)	10.5 ± 0.9	8.2 ± 0.6
(total)	0.14 ± 0.02	0.07 ± 0.01

[a]The above values are differentials taken from the lavage of rats used for the alveolar macrophage phagocytosis assay (N = 12 per group), and the total numbers are given x 10^6 cells.

Table I-5

Macrophage Differential for Lung Lavage Fluid[a]
(Mean ± SE)

Aerosol Concentration of Cu-Zn Alloy	Evaluation Time: End of Exposure	Evaluation Time: After Recovery
Phase III, Part 1		
1.0 mg/m^3 (percent)	90.3 ± 1.5	91.6 ± 1.2
(total)	0.80 ± 0.08	1.07 ± 0.08
3.2 mg/m^3 (percent)	85.8 ± 1.0	87.2 ± 1.4
(total)	1.25 ± 0.15	1.11 ± 0.12
10.0 mg/m^3 (percent)	81.0 ± 1.4	86.2 ± 1.5
(total)	2.56 ± 0.31	0.82 ± 0.11
Phase III, Part 2		
Sham (percent)	90.1 ± 1.9	92.1 ± 1.0
(total)	0.93 ± 0.05	0.96 ± 0.04
0.32 mg/m^3 (percent)	92.4 ± 1.1	91.6 ± 1.3
(total)	0.87 ± 0.02	0.87 ± 0.07
3.2 mg/m^3 (percent)	87.3 ± 1.0	91.5 ± 0.6
(total)	1.10 ± 0.08	0.82 ± 0.05

[a]The above values are differentials taken from the lavage of rats used for the alveolar macrophage phagocytosis assay. N = 12 per group and the total numbers are given x 10^6 cells.

Table I-6

Collagen in Lavage Fluid After 13-Week Exposure to Cu-Zn Alloy Powder and After 4-Week Recovery Period (N = 12, Values are Mean ± SE)

Aerosol Concentration of Cu-Zn Alloy	Evaluation Time: End of Exposure, µg/g Control Lung Weight	End of Exposure, µg/kg Body Weight	After Recovery, µg/g Control Lung Weight	After Recovery, µg/kg Body Weight
Phase III, Part 1				
1.0 mg/m^3	63.5 ± 6.0	313 ± 34	68.0 ± 6.8	306 ± 32
3.2 mg/m^3	59.8 ± 4.2[a]	288 ± 24[a]	64.1 ± 3.6	281 ± 18
10.0 mg/m^3	84.4 ± 6.2	437 ± 38	57.4 ± 3.0	265 ± 20
Phase III, Part 2				
0 (Sham)	45.4 ± 2.8	216 ± 18	47.6 ± 4.2	199 ± 25
0.32 mg/m^3	48.6 ± 2.3	229 ± 15	61.4 ± 9.7	249 ± 33
3.2 mg/m^3	55.1 ± 4.6[a]	264 ± 27[a]	44.9 ± 2.2	189 ± 14

[a]N = 11.

Table I-7

Total Lung Collagen[a] After 13-Week Exposure to Cu-Zn Alloy Powder and After 4-Week Recovery Period (Mean ± SE)

Aerosol Concentration of Cu-Zn Alloy	N	Evaluation Time: End of Exposure		Evaluation Time: After Recovery	
		mg/g Control Lung Weight	mg/kg Body Weight	mg/g Control Lung Weight	mg/kg Body Weight
Phase III, Part 1					
3.2 mg/m^3	10	18.1 ± 0.5	88 ± 3		
10.0 mg/m^3	10	18.9 ± 0.8	97 ± 5	17.5 ± 1.1	80 ± 6
Phase III, Part 2					
0 (Sham)	6	17.2 ± 1.2	82 ± 8	17.6 ± 1.3	72 ± 9
0 (Sham)[b]	12	17.4 ± 0.8	77 ± 6		
3.2 mg/m^3	10	19.3 ± 1.0	91 ± 5		

[a]All samples analyzed as a batch after collection of samples for Phase III, Part 2.

[b]Results combined for shams evaluated at the end of exposure and after the 4-week recovery period.

Table I-8

Immunology Results for Tracheobronchial Lymph Nodes from Rats in Phase III, Parts 1 and 2
(Values are Mean ± SE; N = 6-8)

Aerosol Concentration of Cu-Zn Alloy	Total Lymphoid Cells x 10^{-6}		Antibody-Forming Cells Per Million Lymphocytes		Total Antibody-Forming Cells	
	EOE	REC	EOE	REC	EOE	REC
Phase III, Part 1						
1.0 mg/m^3	8.21 ± 1.11	9.40 ± 1.72	1080 ± 327	907 ± 313	9360 ± 3490	10250 ± 5020
3.2 mg/m^3	15.93 ± 2.60	7.51 ± 0.66	887 ± 133	394 ± 144	14700 ± 3280	2980 ± 992
10.0 mg/m^3	27.09 ± 3.43	10.09 ± 0.51	884 ± 115	369 ± 115	23300 ± 3540	3927 ± 1290
Phase III, Part 2						
0 (Sham)	8.78 ± 0.71	10.00 ± 0.71	517 ± 104	1110 ± 237	4840 ± 1170	11200 ± 2740
3.2 mg/m^3	15.28 ± 1.46	8.54 ± 1.27	346 ± 83	493 ± 131	5570 ± 1340	5290 ± 1850

Table I-9

Macrophage Phagocytosis of Erythrocytes[a]
(Mean ± SE)

Aerosol Concentration of Cu-Zn Alloy	Evaluation Time: End of Exposure	Evaluation Time: After Recovery
Phase III, Part 1		
1.0 mg/m^3	481 ± 30	341 ± 30
3.2 mg/m^3	331 ± 12	289 ± 39
10.0 mg/m^3	251 + 16	299 ± 16
Phase III, Part 2		
0 (Sham)	367 ± 20	404 ± 27
0.32 mg/m^3	490 ± 25	395 ± 32
3.2 mg/m^3	467 ± 26	417 + 31

[a]The above values show the mean and SE of number of erythrocytes phagocytized by 100 macrophages (N = 12).

Table I-10

Percentages of Macrophages that Phagocytized Erythrocytes[a]
(Mean ± SE)

Aerosol Concentration of Cu-Zn Alloy	Evaluation Time	
	End of Exposure	After Recovery
Phase III, Part 1		
1.0 mg/m^3	80.5 ± 1.5	76.0 ± 2.1
3.2 mg/m^3	67.3 ± 2.5[b]	72.9 ± 2.8
10.0 mg/m^3	60.2 ± 3.6[b]	73.2 ± 1.9
Phase III, Part 2		
0 (Sham)	74.4 ± 1.9	81.8 + 2.5
0.32 mg/m^3	79.9 ± 1.2	82.0 ± 2.2
3.2 mg/m^3	76.6 ± 2.1	85.6 ± 2.2

[a]The above values show the mean and SE of the percent macrophages that have phagocytized one or more erythrocytes (N = 12 per group).

Table I-11

Pulmonary Function Results for Rats in Phase III, Parts 1 and 2 (Baseline Measurements)
(Values are Mean ± SE; N = 16)

Parameter	Units	Aerosol Concentration of Powdered Cu-Zn Alloy, mg/m^3					
		Phase III, Part 1				Phase III, Part 2	
		0 (Sham)	1.0	3.2	10	0 (Sham)	3.2
Total Lung Capacity (TLC)	mL	11.4 ± 0.4	11.1 ± 0.4	11.4 ± 0.4	11.1 ± 0.3	9.5 ± 0.4	10.3 ± 0.3
Vital Capacity/TLC	percent	86.4 ± 0.9	87.7 ± 0.8	86.3 ± 0.9	87.6 ± 0.7	91.2 ± 1.4	89.5 ± 0.9
Functional Residual Capacity	mL	2.5 ± 0.1	2.3 ± 0.1	2.6 ± 0.1	2.4 ± 0.1	1.9 ± 0.1	2.1 ± 0.1
Dynamic Lung Compliance	mL/cm H_2O	0.43 ± 0.03	0.42 ± 0.03	0.45 ± 0.04	0.41 ± 0.03	0.43 ± 0.05	0.48 ± 0.06
Quasistatic Chord Compliance	mL/cm H_2O	0.65 ± 0.02	0.64 ± 0.02	0.66 ± 0.03	0.63 ± 0.02	0.53 ± 0.02	0.58 ± 0.02
CO Diffusing Capacity (DLCO)	mL/min/mm Hg	0.18 ± 0.01	0.19 ± 0.01	0.18 ± 0.01	0.19 ± 0.01	0.19 ± 0.01	0.19 ± 0.01
DLCO/Lung Volume	DLCO/mL	0.017 ± 0.001	0.017 ± 0.001	0.017 ± 0.001	0.018 ± 0.001	0.018 ± 0.001	0.018 ± 0.001
DLCO/kg Body Weight	DLCO/kg	0.81 ± 0.03	0.85 ± 0.03	0.81 ± 0.02	0.83 ± 0.02	0.80 ± 0.03	0.78 ± 0.04
Forced Vital Capacity Exhaled in 0.1 Second	percent	71.8 ± 1.4	72.8 ± 2.0	70.5 ± 3.1	71.9 ± 2.8	75.8 ± 1.5	73.2 ± 1.5
Mean Midexpiratory Flow (MMEF)	mL/sec	68.5 ± 3.4	72.6 ± 4.1	69.5 ± 5.5	70.9 ± 5.3	65.9 ± 2.8	68.8 ± 2.9
MMEF/Forced Vital Capacity	mL/sec/mL	6.9 ± 0.3	7.3 ± 0.4	6.9 ± 0.6	7.1 ± 0.6	7.9 ± 0.4	7.5 ± 0.4
Slope of Phase III of Single-Breath N_2 Washout	percent N_2/mL	102.6 ± 16	97.3 ± 5.5	95.4 ± 7.5	98.7 ± 6.1	68.9 ± 4.0	66.1 ± 3.9

Table I-12

Pulmonary Function Results for Rats in Phase III, Parts 1 and 2 (Week Seven of Exposures)
(Values are Mean ± SE; N = 16)

Parameter	Units	Aerosol Concentration of Powdered Cu-Zn Alloy, mg/m^3					
		Phase III, Part 1				Phase III, Part 2	
		0 (Sham)	1.0	3.2	10	0 (Sham)	3.2
Total Lung Capacity (TLC)	mL	11.6 ± 0.4	11.4 ± 0.4	11.7 ± 0.5	11.1 ± 0.3	12.6 ± 0.9	13.1 ± 0.7
Vital Capacity/TLC	percent	93.2 ± 0.5	91.6 ± 0.7	92.4 ± 0.7	91.1 ± 0.7	92.4 ± 0.6	91.5 ± 0.7
Functional Residual Capacity	mL	2.2 ± 0.1	2.2 ± 0.1	2.3 ± 0.1	2.3 ± 0.1	2.5 ± 0.2	2.6 ± 0.1
Dynamic Lung Compliance	mL/cm H_2O	0.45 ± 0.04	0.41 ± 0.04	0.46 ± 0.04	0.39 ± 0.03	0.47 ± 0.04	0.51 ± 0.04
Quasistatic Chord Compliance	mL/cm H_2O	0.70 ± 0.03	0.66 ± 0.03	0.69 ± 0.03	0.64 ± 0.02	0.74 ± 0.05	0.79 ± 0.05
CO Diffusing Capacity (DLCO)	mL/min/mm Hg	0.21 ± 0.01	0.21 ± 0.01	0.21 ± 0.01	0.18 ± 0.02	0.21 ± 0.01	0.21 ± 0.01
DLCO/Lung Volume	DLCO/mL	0.018 ± 0.001	0.019 ± 0.001	0.018 ± 0.001	0.016 ± 0.001	0.019 ± 0.001	0.018 ± 0.001
DLCO/kg Body Weight	DLCO/kg	0.92 ± 0.03	0.92 ± 0.02	0.93 ± 0.03	0.83 ± 0.02	0.86 ± 0.03	0.89 ± 0.03
Forced Vital Capacity Exhaled in 0.1 Second	percent	70.8 ± 1.3	69.4 ± 2.3	67.4 ± 2.4	72.7 ± 1.6	71.4 ± 1.5	70.8 ± 1.3
Mean Midexpiratory Flow (MMEF)	mL/sec	78.3 ± 3.2	76.4 ± 4.5	72.4 ± 4.9	78.1 ± 2.3	80.3 ± 4.6	81.9 ± 3.8
MMEF/Forced Vital Capacity	mL/sec/mL	6.9 ± 0.3	6.8 ± 0.4	6.5 ± 0.5	7.4 ± 0.3	7.0 ± 0.3	7.0 ± 0.2
Slope of Phase III of Single-Breath N_2 Washout	percent N_2/mL	75.7 ± 5.6	82.6 ± 5.8	79.4 ± 4.6	81.4 ± 4.9	67.9 ± 3.4	65.6 ± 4.3

Table I-13

Pulmonary Function Results for Rats in Phase III, Parts 1 and 2 (End of Exposure)
(Values are Mean ± SE; N = 16)

		Aerosol Concentration of Powdered Cu-Zn Alloy, mg/m^3				
		Phase III, Part 1			Phase III, Part 2	
Parameter	Units	1.0	3.2	10	0 (Sham)	3.2
Total Lung Capacity (TLC)	mL	11.7 ± 0.4	12.0 ± 0.5	11.2 ± 0.5	11.4 ± 0.5	11.2 ± 0.4
Vital Capacity/TLC	percent	93.3 ± 0.9	94.4 ± 0.7	92.2 ± 0.7	91.9 ± 1.1	92.7 ± 0.8
Functional Residual Capacity	mL	2.1 ± 0.1	2.1 ± 0.1	2.1 ± 0.1	2.2 ± 0.1	2.1 ± 0.1
Dynamic Lung Compliance	mL/cm H_2O	0.40 ± 0.02	0.47 ± 0.03	0.37 ± 0.03	0.41 ± 0.03	0.39 ± 0.03
Quasistatic Chord Compliance	mL/cm H_2O	0.71 ± 0.03	0.77 ± 0.04	0.68 ± 0.03	0.68 ± 0.03	0.68 ± 0.02
CO Diffusing Capacity (DLCO)	mL/min/mm Hg	0.22 ± 0.01	0.25 ± 0.02	0.20 ± 0.01	0.25 ± 0.01	0.24 ± 0.01
DLCO/Lung Volume	DLCO/mL	0.018 ± 0.001	0.019 ± 0.001	0.016 ± 0.001	0.020 ± 0.001	0.020 ± 0.001
DLCO/kg Body Weight	DLCO/kg	0.92 ± 0.04	0.97 ± 0.03	0.80 ± 0.03	0.96 ± 0.03	0.95 ± 0.03
Forced Vital Capacity Exhaled in 0.1 Second	percent	67.5 ± 2.2	64.6 ± 1.5	64.8 ± 2.5	73.1 ± 1.8	69.4 ± 2.2
Mean Midexpiratory Flow (MMEF)	mL/sec	73.8 ± 5.2	67.0 ± 3.8	63.6 ± 5.0	73.7 ± 2.0	69.6 ± 4.6
MMEF/Forced Vital Capacity	mL/sec/mL	6.4 ± 0.4	5.7 ± 0.3	5.9 ± 0.5	7.4 ± 0.4	6.7 ± 0.4
Slope of Phase III of Single-Breath N_2 Washout	percent N_2/mL	67.4 ± 5.9	69.4 ± 8.3	69.4 ± 6.6	70.0 ± 5.4	69.6 ± 5.4

Table I-14

Pulmonary Function Results for Rats in Phase III, Parts 1 and 2 (After 4-Week Recovery Period)
(Values are Mean ± SE; N = 16)

Parameter	Units	Aerosol Concentration of Powdered Cu-Zn Alloy, mg/m^3				
		Phase III, Part 1			Phase III, Part 2	
		1.0	3.2	10	0 (Sham)	3.2
Total Lung Capacity (TLC)	mL	12.5 ± 0.5	13.1 ± 0.7	12.7 ± 0.5	11.2 ± 0.4	11.7 ± 0.5
Vital Capacity/TLC	percent	88.9 ± 0.9	88.9 ± 0.9	88.6 ± 0.7	93.1 ± 0.8	92.0 ± 0.8
Functional Residual Capacity	mL	2.7 ± 0.1	2.7 ± 0.1	2.7 ± 0.1	2.1 ± 0.1	2.3 ± 0.1
Dynamic Lung Compliance	mL/cm H_2O	0.43 ± 0.04	0.45 ± 0.05	0.40 ± 0.04	0.39 ± 0.03	0.43 ± 0.03
Quasistatic Chord Compliance	mL/cm H_2O	0.75 ± 0.03	0.77 ± 0.04	0.78 ± 0.03	0.68 ± 0.02	0.70 ± 0.02
CO Diffusing Capacity (DLCO)	mL/min/mm Hg	0.26 ± 0.02	0.26 ± 0.02	0.25 ± 0.02	0.24 ± 0.02	0.24 ± 0.01
DLCO/Lung Volume	DLCO/mL	0.021 ± 0.001	0.019 ± 0.001	0.020 ± 0.001	0.019 ± 0.001	0.019 ± 0.001
DLCO/kg Body Weight	DLCO/kg	0.88 ± 0.06	0.74 ± 0.06	0.84 ± 0.05	0.88 ± 0.03	0.91 ± 0.03
Forced Vital Capacity Exhaled in 0.1 Second	percent	67.9 ± 1.7	65.4 ± 2.4	70.8 ± 1.8	67.8 ± 2.5	65.5 ± 2.8
Mean Midexpiratory Flow (MMEF)	mL/sec	77.7 ± 2.7	77.2 ± 5.8	84.7 ± 2.5	65.8 ± 4.7	64.8 ± 6.0
MMEF/Forced Vital Capacity	mL/sec/mL	6.4 ± 0.3	6.1 ± 0.5	7.0 ± 0.3	6.5 ± 0.5	6.0 ± 0.5
Slope of Phase III of Single-Breath N_2 Washout	percent N_2/mL	63.2 ± 5.4	60.6 ± 6.8	57.0 ± 4.4	65.0 ± 4.5	66.8 ± 3.6

Table I-15

Summary of Respiratory Tract Lesions in F344/N Rats
After 13-Week Exposure to Aerosols of Cu-Zn Alloy Powder
(End of Exposure)

	Phase III, Part 1			Phase III, Part 2		
Lesion	1.0[a]	3.2	10	Sham	0.32	3.2
Nasal Epithelium Atrophy	3/22[b] (1)[c]	3/22 (1)	15/22 (1.2)	0	0	3/22 (1)
Alveolar Macrophage Hyperplasia	0	14/22 (1)	18/22 (1.4)	1/22 (1)	0	10/22 (1)
Type II Pneumocyte Hyperplasia	0	7/22 (1)	17/22 (1.2)	0	0	5/22 (1)
Alveolitis	0	7/22 (1)	18/22 (1.4)	0	0	4/22 (1)

[a]Concentration of exposure atmosphere of Cu-Zn alloy powder, mg/m^3.

[b]Fraction of rats with lesion.

[c]Average severity score for animals with induced lesions: 0 = no changes relative to normal, lesion not present; 1 = slight degree of changes, or small amount present, mild response; 2 = moderate, median, or middle severity or amount; 3 = marked severity or degree of changes, large amount present.

Table I-16

Summary of Respiratory Tract Lesions in F344/N Rats After 4-Week Recovery Period Following Exposure to Aerosols of Cu-Zn Alloy Powder (After Recovery)

	Phase III, Part 1			Phase III, Part 2		
Lesion	1.0[a]	3.2	10	Sham	0.32	3.2
Nasal Epithelium Atrophy	0[b]	1/21 (1)[c]	7/22 (1.4)	0	0	0
Alveolar Macrophage Hyperplasia	0	5/21 (1)	22/22 (1)	3/22 (1)	1/22 (1)	5/22 (1)
Type II Pneumocyte Hyperplasia	1/22 (1)	4/21 (1)	22/22 (1)	0	1/22 (1)	4/22 (1)
Alveolitis	0	0	0	0	1/22 (1)	1/22 (1)

[a]Concentration of exposure atmosphere of Cu-Zn alloy powder, mg/m^3.

[b]Fraction of rats with lesions.

[c]Average severity score for animals with induced lesions: defined in Table I-15.

Table I-17

Summary Results for Statistical[a] Comparisons for Endpoint Evaluations at the End of Exposure and After a 4-Week Recovery Period for F344/N Rats Exposed to 3.2 mg Cu-Zn/m^3 in Phase III, Parts 1 and 2

Evaluation	N[b]	Sacrifice Time: End of Exposure, Part 1	End of Exposure, Part 2	Sig	After Recovery, Part 1	After Recovery, Part 2	Sig
β-Glucuronidase in BALF, mIU	12	1.84 ± 0.23	1.39 ± 0.22	NS	1.79 ± 0.26	1.11 ± 0.13	NS
Alkaline Phosphatase in BALF, mIU	12	469 ± 39	387 ± 38	NS	293 ± 18	215 ± 17	NS
Lactate Dehydrogenase in BALF, mIU	12	1658 ± 165	571 ± 63	0.01	827 ± 144	406 ± 30	0.05
Total Protein in BALF, mg	12	1.87 ± 0.10	1.54 ± 0.12	NS	1.04 ± 0.14	1.34 ± 0.11	NS
Total Cells in BALF x 10^{-6}	12	1.44 ± 0.16	1.26 ± 0.10	NS	1.26 ± 0.14	0.89 ± 0.05	NS
Neutrophils in BALF, Percent	12	4.48 ± 0.70	2.03 ± 0.56	NS	0.59 ± 0.24	0.33 ± 0.11	NS
Neutrophils in BALF, Total x 10^{-6}	12	0.060 ± 0.009	0.027 ± 0.008	NS	0.007 ± 0.002	0.003 ± 0.001	NS
Lymphocytes in BALF, Percent	12	9.2 ± 1.3	10.5 ± 0.9	NS	12.0 ± 1.4	8.2 ± 0.6	NS
Lymphocytes in BALF, Total x 10^{-6}	12	0.13 ± 0.02	0.14 ± 0.02	NS	0.15 ± 0.03	0.07 ± 0.01	NS
Macrophages in BALF, Percent	12	85.8 ± 0.9	87.3 ± 1.0	NS	87.2 ± 1.4	91.5 ± 0.6	NS
Macrophages in BALF, Total x 10^{-6}	12	1.25 ± 0.15	1.10 ± 0.08	NS	1.11 ± 0.12	0.82 ± 0.05	NS
Collagen in BALF, μg/g Control Lung	d	59.8 ± 4.2	55.1 ± 4.6	NS	64.1 ± 3.6	44.9 ± 2.2	0.01
Collagen in BALF, μg/kg Body Weight	d	288.3 ± 23.7	264.4 ± 26.9	NS	281.4 ± 17.9	188.7 ± 14.1	0.05
Total Lung Collagen, mg/g Control Lung	10	18.1 ± 0.5	19.3 ± 1.0	NS			
Total Lung Collagen, mg/kg Body Weight	10	88 ± 3	91 ± 5	NS			
Total Lymphoid Cells, x 10^{-6}	15	15.9 ± 2.6	15.3 ± 1.5	NS	7.5 ± 0.7	8.5 ± 1.3	NS
Antibody-Forming Cells per Million Lymphocytes	15	887 ± 133	346 ± 83	0.01	394 ± 144	493 ± 131	NS
Total Antibody-Forming Cells	15	14650 ± 3277	5569 ± 1340	0.01	2980 ± 992	5288 ± 1850	NS
RBC Phagocytized per 100 Macrophages	12	331 ± 12	467 ± 26	0.01	289 ± 39	417 ± 31	NS
Percent of Macrophages that Phagocytized RBC	12	67.3 ± 2.5	76.6 ± 2.1	NS	72.9 ± 2.8	85.6 ± 2.2	NS

Table I-17 (Cont.)

Summary Results for Statistical[a] Comparisons for Endpoint Evaluations at the End of Exposure and After a 4-Week Recovery Period for F344/N Rats Exposed to 3.2 mg Cu-Zn/m^3 in Phase III, Parts 1 and 2

Evaluation	N[b]	End of Exposure Part 1	End of Exposure Part 2	End of Exposure Sig	After Recovery Part 1	After Recovery Part 2	After Recovery Sig
Total Lung Capacity (TLC), mL	16	12.0 ± 0.5	11.3 ± 0.4	NS	13.1 ± 0.7	11.7 ± 0.5	NS
Vital Capacity/TLC (VC/TLC), Percent	16	94.6 ± 0.7	92.6 ± 0.8	NS	89.0 ± 0.9	92.0 ± 0.8	NS
Functional Residual Capacity (FRC), mL	16	2.1 ± 0.1	2.1 ± 0.1	NS	2.7 ± 0.1	2.3 ± 0.1	NS
Dynamic Lung Compliance (CDYN), mL/cm H_2O	16	0.47 ± 0.03	0.39 ± 0.03	NS	0.45 ± 0.05	0.43 ± 0.03	NS
Quasistatic Chord Compliance (CCORD), mL/cm H_2O	16	0.77 ± 0.04	0.68 ± 0.02	NS	0.77 ± 0.04	0.70 ± 0.02	NS
CO Diffusing Capacity (DLCO), mL/min/mm Hg	16	0.25 ± 0.02	0.24 ± 0.01	NS	0.19 ± 0.01	0.24 ± 0.01	0.01
DLCO/Lung Volume, DLCO/mL	16	0.020 ± 0.001	0.022 ± 0.001	NS	0.015 ± 0.001	0.021 ± 0.001	0.01
DLCO/kg Body Weight, DLCO/kg	16	0.97 ± 0.03	0.95 ± 0.03	NS	0.74 ± 0.06	0.91 ± 0.03	NS
Forced Vital Capacity Exhaled in 0.1 Second (FEV1), Percent	16	64.6 ± 1.5	69.4 ± 2.2	NS	65.4 ± 2.4	65.5 ± 2.8	NS
Mean Midexpiratory Flow (MMEF), mL/Second	16	67.0 ± 4.0	69.6 ± 4.6	NS	77.2 ± 5.8	64.8 ± 6.0	NS
MMEF/Forced Vital Capacity, mL/Second/mL	16	5.7 ± 0.3	6.7 ± 0.4	NS	6.1 ± 0.5	6.0 ± 0.5	NS
Slope of Phase III of Single-Breath N_2 Washout, Percent N_2/mL	16	69.4 ± 8.3	69.6 ± 5 4	NS	60.6 ± 6.8	66.8 ± 3.6	NS
Nasal Epithelium Atrophy, Severity Score	21 or 22	0.14 ± 0.08	0.14 ± 0 08	NS	0.05 ± 0.05	0	NS
Alveolar Macrophage Hyperplasia, Severity Score	21 or 22	0.64 ± 0.11	0.46 ± 0.11	NS	0.24 ± 0.10	0.23 ± 0.09	NS
Type II Pneumocyte Hyperplasia, Severity Score	21 or 22	0.32 ± 0.10	0.23 ± 0.09	NS	0.19 ± 0.09	0.18 ± 0.08	NS
Alveolitis, Severity Score	21 or 22	0.32 ± 0.10	0.18 ± 0.08	NS	0	0.05 ± 0.05	NS

[a]The groups exposed to 3.2 mg Cu-Zn/m^3 in Parts 1 and 2 were compared using Student's t-test for unequal variances when Levene's test indicated the variances were not the same. When Levene's test did not show differences between the variances, Student's t-test for equal variances was used. Probability values were adjusted for multiple comparisons using Bonferroni's inequality.

[b]N = The same for Phase III, Parts 1 and 2.

[c]The values for lactate dehydrogenase (LDH) were higher for all groups in Phase III, Part 1 than they were for groups in Phase III, Part 2. The values for LDH in the sham-exposed rats in Phase III, Part 2 were in agreement with historical control values. Therefore, the LDH values for Phase III, Part 1 were considered invalid and were ignored in evaluating the combined results from Phase III, Parts 1 and 2.

[d]N = 11 at end of exposure; N = 12 after the recovery period.

J. MISCELLANEOUS

Continental Grain Co.

CERTIFICATE OF FEED ANALYSIS

PLANT NO. 010/738

FEED NO. 8728.00 CATEGORY NO. Cont Postbant BL-1

☐ ROUTINE ☒ SPECIAL STUDY ☐ NON-ROUTINE

DATE MFG. 7/23/86 RUN OR BATCH NO. PC7236-1

ANALYSIS: LAB NO. 5665

	GUAR	CALC.	ASSAY
PROT.			25.3
MOIST.			9.55
ASH			6.90
FAT			4.51
FIBER			4.09
Ca			1.19
P			.92
SALT			.76
N.P.N.			
VIT A			
THIAMINE			

Please grind
1 - 5 LB
1 - 1 LB

REMARKS:

DATE RECEIVED 7-24-86

ANALYST ______ DATE COMPLETED ______

RES-19C

RECEIPT

ASSAY DONE
APPROVED BY R&D LAB MGR: [handwritten initials] 27-OCT-86
DISTRIBUTE TO ROB BEVERLY

----------------------- ASSAY = R5665 -----------------------

DATE AS FED

PLANT	FEED	TYPE	MFG-DATE	BATCH NO	COMMENT----------------COMMENT
010	872800	SPECIAL	860723	P07236-1	

RESULTS

TEST	UNITS	FED	DRY	C-VAL	GUAR-VAL
VITAMIN A	IU/L	8998.000	0.000		
THIAMINE	MG/L	4.400	0.000		

SPECIMEN	SPECIMEN I.D. NUMBER		ACCESSION NO
R-5665	0390775		390775

REFERRING CLIENT	DATE COLLECTED	CLIENT LAB NO.	TIME COLLECTED	RECEIVED	REPORTED
CONTINENTAL GRAIN CO.	07/24/86		00:00	07/25/86	
	0775	00000			08/04/86

TEST	RESULT	REFERENCE LIMITS	UNITS
TOTAL FEED SCREEN			
ARSENIC	0.55		PPM
CADMIUM	0.35		PPM
LEAD	0.20		PPM
MERCURY	<0.01		PPM
SELENIUM	0.25		PPM
AFLATOXIN B1	<0.01		PPM
AFLATOXIN B2	<0.01		PPM
AFLATOXIN G1	<0.01		PPM
AFLATOXIN G2	<0.01		PPM
ALDRIN	<0.01		PPM
DIELDRIN	<0.01		PPM
ENDRIN	<0.01		PPM
HEPTACHLOR	<0.01		PPM
HEPTACHLOREPOXIDE	<0.01		PPM
LINDANE	<0.01		PPM
CHLORDANE	<0.01		PPM
DDT RELATED SUBS.	<0.01		
TOXAPHENE	<0.10		PPM
PCBS	<0.10		PPM
DIAZINON	<0.10		PPM
DISULFATON	<0.10		PPM
ETHION	<0.10		PPM
MALATHION	0.33		PPM
METHYL PARATHION	<0.10		PPM
PARATHION	<0.10		PPM
THIMET	<0.10		PPM
THIODAN	<0.10		PPM
TRITHION	<0 10		PPM
CAROTENE	5.91		PPM
NITROGEN, NITRATE	74		PPM
NITROGEN, NITRITE	<1		PPM
STANDARD PLATE COUNT	34000		
COLIFORMS, FECAL	0		COL/DL
E. COLI	0		MPN
BHA	<1		PPM
BHT	<1		PPM
NITROSAMINES	<1		MCG/L
ALPHA BHC	<0.01		PPM

SPECIMEN	SPECIMEN I.D. NUMBER		ACCESSION N
R-5665	0390775		390775

REFERRING CLIENT	DATE COLLECTED	CLIENT LAB NO.	TIME COLLECTED	RECEIVED	REPORTED
CONTINENTAL GRAIN CO.	07/24/86		00:00	07/25/8	08/04/8
	0775	00000			

TEST	RESULT	REFERENCE LIMITS	UNITS
BETA BHC	<0.01		PPM
DELTA BHC	<0.01		PPM
4,4'DDE	<0.01		PPM
4,4'DDD	<0.01		PPM
HCB	<0.01		PPM
MIREX	<0.10		PPM
METHOXYCHLOR	<0.10		PPM
TELODRIN	<0.10		PPM
RONNEL	<0.10		PPM
ETHYL PARATHION	<0.10		PPM
ALPHA ENDOSULFAN	<0.10		PPM
BETA ENDOSULFAN	<0.10		PPM
ENDOSULFAN SULFATE	<0.10		PPM

XIII. LIST OF PUBLICATIONS

None

XIV. PERSONNEL SUPPORTED BY PROJECT

Name	Duty
Snipes, M. B., Ph.D.	Principal investigator responsible for coordination of activities in the project.
Bice, D. E., Ph.D.	Immunology and phagocytosis evaluations.
Burt, D. G., D.V.M.	Small animal care operations.
Damon, E. G., Ph.D.	Data management in Path/Tox Data Base System.
Eidson, A. F., Ph.D.	Coordinator for activities associated with analytical techniques used in this project.
Hahn, F. F., D.V.M., Ph.D.	Pathology evaluations.
Harkema, J. R., D.V.M., Ph.D.	Pathology evaluations.
Harris, D. L., M.S.	Quality Assurance
Henderson, R. F., Ph.D.	Biochemistry evaluations
Hobbs, C. H., D.V.M.	Veterinarian for project and member of the ITRI Directorate in charge of this research.
Mauderly, J. L., D.V.M., Ph.D.	Respiratory function evaluations.
Pickrell, J. A., D.V.M., Ph.D.	Blood chemistry evaluations.
Seiler, F. A., Ph.D.	Statistician for project.
Yeh, H. C., Ph.D.	Responsible for aerosol science activities.

XV. DISTRIBUTION LIST

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